



Association of Korean Neuroscientists

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5th AKN 2024 Research Symposium Summary

April 26-27, 2024, Baylor College of Medicine, Houston TX

AKN 2024 Research Symposium



Association of
Korean Neuroscientists

대한미국의인신경과학회



Consulate General of the Republic of Korea



Meeting Program

Symposium Day 1

- 1:00 – 1:40 Registration (NRI 7F desk)
- 1:40 – 1:50 Welcome Remark (Yoon-Seong Kim, AKN President)
- 1:50 – 2:00 Greetings from the Consulate General of the Republic of Korea in Houston
- 2:00 – 3:00 Plenary lecture (moderator: Jun-Ho La)
The ugly history of Alzheimer's disease research & the new movement toward a clearer future
Jungsu Kim, Indiana University
- 3:00 – 4:15 Short-talks: **Neurodegeneration (I)** (moderator: Jun-Ho La)
- 4:15 – 4:30 GenDEPOT Sponsorship acknowledgment (moderator: Yoon-Seong Kim)
Kyle Yun and Jihye Na, GenDEPOT
- 4:30 – 5:00 Break & poster session preparation
- 5:00 – 6:00 Poster session
- 6:00 – Dinner & Networking (moderator: Jun-Ho La)

Symposium Day 2

- 08:00 – 08:50 Breakfast & Networking
- 08:50 – 09:00 Welcome
- 09:00 – 09:45 Keynote session (I) (moderator: Jun-Ho La)
My career in sensory neuroscience and AKN
Jin Mo Chung, University of Texas Medical Branch (UTMB) at Galveston
- 09:45 – 10:45 Short-talks: **Sensory neuroscience** (moderator: Jun-Ho La)
- 10:45 – 11:00 Break
- 11:00 – 11:45 Keynote session (II) by the Tong H. Joh Research Innovation Awardee
(moderator: Yoon-Seong Kim)
Double-stranded RNA as a trigger for neuroinflammation
Hachung Chung, Columbia University Medical Center
- 11:45 – 12:00 Special talk (moderator: Hyun Kyoung Lee)
Korea's Global Research Agenda: Trends, Challenges, and Opportunities
Hyewhon Rhim, Korea Institute of Science and Technology (KIST)
- 12:00 – 1:00 Lunch & Networking
- 1:00 – 2:15 AKN-KBRI-Joint meeting: **Multidisciplinary Convergence Cluster for Brain diseases**
(moderator: KiBum Lee, Juhyun Kim)
- 2:15 – 2:30 Break
- 2:30 – 3:15 Short-talks: **Neurodegeneration (II)** (moderator: Jee-Yeon Hwang)
- 3:15 – 4:30 Short-talks: **Synapses, circuits, microenvironment in the brain** (moderator: Hyung-Goo Kim)
- 4:30 – 4:45 Break
- 4:45 – 5:45 Short-talks: **BBB and neuroinflammation** (moderator: Hyun Kyoung Lee)
- 5:45 – 6:00 Poster Award
- 6:00 – Dinner

Meeting Summary



The 5th AKN Research Symposium took place on April 26-27 at the Jan and Dan Duncan Neurological Research Institute (NRI), Baylor College of Medicine, in Houston. Hosted by AKN scientists from Houston and across Texas, this two-day event marked a milestone with approximately 90 neuroscientists from the US and Korea in attendance, the highest number since the symposium's inception in 2018.

The symposium commenced with an inspiring opening plenary lecture by Prof. Jungsu Kim. On the following day, Prof. Jin Mo Chung, a founding member of AKN, delivered a keynote presentation, highlighting his dedication to AKN along with his career path. This year's Tong H. Joh Research Innovation Award was presented to Dr. Hachung Chung from Columbia University Medical Center.

The event was further enriched by the participation of researchers from the Korean Brain Research Institute (KBRI) and the Allen Institute for Brain Science, who shared their groundbreaking studies. Over the course of the symposium, 21 researchers delivered presentations across five short-talk sessions, showcasing a diverse range of cutting-edge neuroscience research.

Trainees had the opportunity to present their projects during the poster session, with three individuals receiving awards for their outstanding posters. The symposium's success was made possible by the efforts of the regional organizing committee and the generous support of sponsors, including the Consulate General of the Republic of Korea, KBRI, GenDEPOT, and Innovaplex.

The 5th AKN Research Symposium provided an excellent platform for networking and exchanging research ideas, fostering collaboration between faculty members and trainees.

Plenary Lecture

“The ugly history of Alzheimer's disease research & the new movement toward a clearer future”



Prof. Jungsu Kim, Ph.D.

*P. Michael Conneally Professor of Medical and Molecular Genetics
Professor, Stark Neurosciences Research Institute
Department of Medical and Molecular Genetics
Indiana University School of Medicine*

Keynote Lecture

“My career in sensory neuroscience and AKN”

Prof. Jin Mo Chung, Ph.D.

*Professor and Chair
Cecil H. and Ida M. Green Distinguished
University Endowed Chair in Neuroscience and
Cell Biology
Department of Neurobiology
The University of Texas Medical Branch*





Tong H. Joh Research Innovation Award

“Double-stranded RNA as a trigger for neuroinflammation”

Dr. Hachung Chung, Ph.D.

Assistant Professor

Department of Microbiology and Immunology

Columbia University



Long 3'UTRs Predispose Neurons to Inflammation by Promoting Immunostimulatory double-stranded RNA Formation

[Science Immunology. 2023 Oct 20; 8\(88\): eadg2979.](#)

Outstanding Poster Award

1st Place



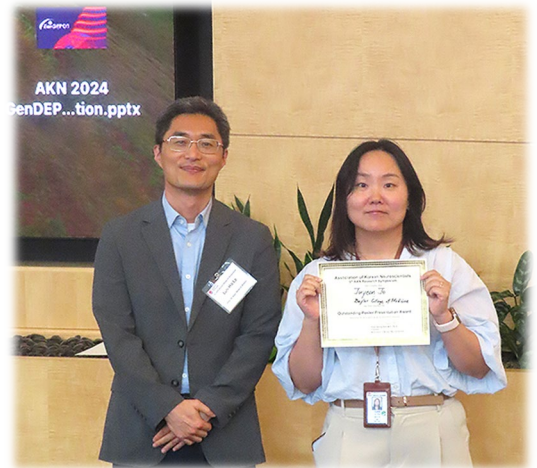
Yejin Park, MS
3-year Graduate student
Baylor College of Medicine
(Hongjie Li lab)

“Beyond the Brain: Alzheimer’s Disease’s Unforeseen Impact on the Peripheral System”

2nd Place

Juyeon Jo, PhD.
Staff Scientist
Baylor College of Medicine
(Hyun K Lee lab)

“Deciphering mechanisms of perinatal white matter injury-induced neuropsychiatric outcomes”



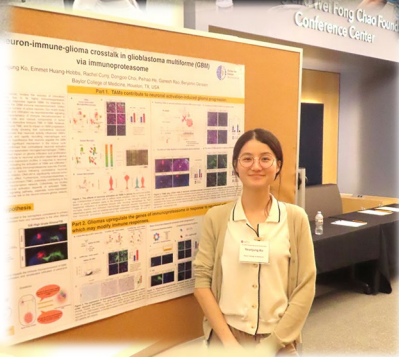
2nd Place

Jung-Wan Mok, Ph.D.
Postdoc
Baylor College of Medicine
(Shinya Yamamoto lab)

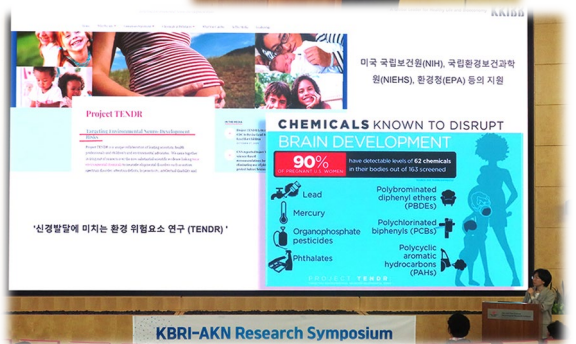
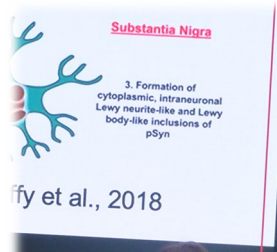
“A de novo gain-of-function variant in the BMPR2 gene induces neurodevelopmental abnormalities”



Photos



Photos



Sponsors



Consulate General
of the Republic of Korea
in Houston



Symposium Committee

Dr. Hyun Kyoung Lee, BCM, symposium co-organizer

Dr. Jun Ho La, UTMB, symposium co-organizer

Dr. Seung-Hee Yoo, UTHSC

Dr. Hyunglok Chung, Methodist Hospital

Dr. Enhee Kim, UTHSC

Dr. Seungwon Choi, UTSW

Meeting Attendees

1	Short talk	Alexa Woo	Assistant Professor	Case Western Reserve University
2	Sponsor	Bernard Lee	Sponsor	Innova Plex
3	Poster	Chorong Han	Postdoc	UTHealth Houston
4	Short talk	Da Yong Lee	Senior Researcher	KRIBB
5	Short talk	Daewoo Lee	Professor	Ohio University
6	Short talk	David E. Kang	Professor	Case Western Reserve University
7	Short talk	Dongjoo Choi	Instructor	Baylor College of Medicine
8		Eunhee Kim	Assistant Professor	UTHealth Houston
9		Eunsu Park	Assistant Professor	UTHealth Houston
10		Eunyoung Lee	Assistant Professor	UTHealth Houston
11		Gab Seok Kim	Assistant Professor	UTHealth Houston
12	Invited Speaker	Hachung Chung (Awardee)	Assistant Professor	Columbia University in the City of New York
13	Poster	Hamin Lee	Students	Baylor College of Medicine
14	Poster	Han Cheon Kim	Research Scientist	UTHealth Houston
15	Poster	Ho Koo	Postdoc	University of Texas Medical Branch
16	Poster	Hye Young Lee	Associate Professor	UTHealth at San Antonio
17	Poster	Hyejin Park	Postdoc	UTHealth Houston
18	Invited Speaker	Hyewhon Rhim (Special talk)	Principal Research Scientist	KIST
19		Hyoung-gon Lee	Associate Professor	University of Texas at San Antonio
20	Short talk	Hyun Kyoung Lee	Associate Professor	Baylor College of Medicine
21		Hyun-Eui Kim	Assistant Professor	UTHealth Houston
22	Short talk	Hyung W. Nam	Associate Professor	LSU Health Sciences Center
23		Hyung-Goo Kim	Associate Professor	Augusta University
24	Short talk	Hyunglok Chung	Assistant Professor	Houston Methodist
25		Hyunyoung Koh	Postdoc	Texas Children's Hospital
26		Jae Kyu Lee	Professor	University of Miami
27	Short talk	Jae Kyung Lee	Associate Professor	University of Georgia
28	Short talk	Jae-Hyun Kim	Postdoc	Baylor College of Medicine
29		Jaebok Wi	Research Assistant	UTHealth at Houston
30	Poster	Jaeyeong Jeong	Postdoc	UTHealth Houston
31	Poster	Jaeyun Sung	Assistant Professor	Mayo Clinic
32		Jee-Yeon Hwang	Assistant Professor	Creighton University
33	Poster	Jeonghoon Oh	Postdoc	Houston Methodist Research Institute
34	Short talk	Jeongyeon Kim	Principal Researcher	Korea Brain Research Institute
35		Ji Ye Lim	Postdoc	UTHealth Houston
36	Sponsor	Jihye Na	Sponsor	GenDEPOT
37	Invited Speaker	Jin Mo Chung (Keynote session)	Professor	UTMB
38		Jinmo Jeong	Postdoc	UT Austin
39		Jongcheon Lim	Postdoc	UTHealth Houston
40		Joo Eun Jung	Assistant Professor	UTHealth Houston
41	Short talk	Juhyun Kim	Senior researcher	한국뇌연구원
42	Short talk	Jun Hee Kim	Professor	University of Michigan, Ann Arbor
43	Short talk	Jun-Ho La	Associate Professor	Univ. of Texas Medical Branch
44		Junyoung Lee	Assistant Professor	UTHealth Houston
45	Poster	Jung-Wan Mok	Postdoc	Baylor College of Medicine
46	Invited Speaker	Jungsu Kim (Plenary lecture)	Professor	Indiana University
47		Junsung Woo	Instructor	Baylor College of Medicine
48	Poster	Junyoung Sonn	Postdoc	Baylor College of Medicine
49		Junyoung Sonn	Postdoc	Baylor College of Medicine
50	Poster	Juyeon Jo	Research Scientist	Baylor College of Medicine
51	Short talk	Kanghoon Jung	Scientist	Allen Institute for Neural Dynamics
52		Kevin (Kyung) Park	Professor	UT Southwestern Medical Center
53	Short talk	KiBum Lee	Professor	Rutgers University
54		Kyeongmin Kim	Postdoc	University of Texas Medical Branch
55	Sponsor	Kyle Yun	Sponsor	GenDEPOT
56	Short talk	Kyung-An Han	Professor	The University of Texas at El Paso
57	Short talk	Meanhwan Kim	Senior Scientist	Allen Institute for Brain Science
58	Short talk	Mi-Hyeon Jang	Associate Professor	Rutgers University
59		Sang Hun Lee	Assistant Professor	Colorado State University
60		Sangyoung Kim	Staff	Korea Brain Research Institute (KBRI)
61	Poster	Seo-Jun Kang	Postdoc	UTHealth at San Antonio
62	Short talk	Seonil Kim	Associate Professor	Colorado State University
63	Short talk	Seung-Hee Yoo	Associate Professor	UTHealth Houston
64	Short talk	Seungwon Choi	Assistant Professor	UT Southwestern Medical Center
65	Sponsor	Sinae Sung	Consul	Consul
66		Sodam Kim	Postdoc	UTHealth Houston
67		Sun Young Kim	Graduate student	UTHealth Houston
68	Short talk	Sung Soo Kim	Assistant Professor	UC Santa Barbara
69		Sung Yun Jung	Associate Professor	Baylor College of Medicine
70	Poster	Ukbong Kwon	Postdoc	Baylor College of Medicine
71	Short talk	Y. Hwan Kim	Professor	Delaware State University
72	Poster	Ye-Jin Park	Students	Baylor College of Medicine
73	Poster	Yeuniung Ko	Students	Baylor College of Medicine
74	Short talk	Yong Kim	Associate Professor	Rutgers University
75	Short talk	Yoon-Seong Kim	Professor	Rutgers University
76	Poster	Yoonhee Ki	Students	Baylor College of Medicine
77		Yoonsuck Choe	Professor	Texas A&M University
78		Young-Jin Son	Professor	Temple University
79	Poster	Youngdoo kim	Postdoc	Baylor College of Medicine
80	Poster	Yunseon Yang	Postdoc	Houston Methodist
81	On-site	Hyun-Hwan Jeong	Associate Professor	Baylor College of Medicine
82		Joo Hyun Kim	Postdoc	Baylor College of Medicine
83		Hwanyoung Back	Research Assistant	UTHealth Houston
84		Songmi Lee	Student	UTHealth Houston
85		Chai Jin Lee	Postdoc	Baylor College of Medicine
86		Yeun Kim	Postdoc	Baylor College of Medicine



Association of Korean Neuroscientists



Dr. Alexa Woo

Assistant Professor

Department of Pathology at Case Western Reserve University

Email: jaw330@case.edu

Lab website: <https://www.kang-lab.com/Woo%20members.html>

A. Research Focus and established techniques: Alzheimer's Disease (AD) and related dementias; tauopathies, lewy body diseases, and other neurodegenerative diseases

- **Molecular mechanisms and therapeutic targeting of beta-arrestins in ADRDs:** We utilize interdisciplinary approaches, including the cell biology of neurons, live-cell imaging of genetically encoded fluorescent reporters, genetic models of AD/ADRD, recombinant AAVs, electrophysiology, and behavior analysis, to explore the previously unexamined role of beta-arrestins in neurodegeneration associated with AD and ADRDs. (Relevant tools can be found in PMID: 32071246, 34862271)
- **Mitochondrial protein CHCHD2 in Lewy body disorders:** Rare mutations in the gene coding for the mitochondrial protein CHCHD2 are associated with Parkinson's Disease (PD) and other Lewy body disorders. By employing a multidisciplinary approach both in vitro and in vivo, we aim to reveal how pathological CHCHD2 contributes to the pathogenesis of PD and other Lewy body disorders. (Relevant tools can be found at: PMID:)
- **Mitochondrial protein CHCHD2 vs CHCHD10 in neurodegenerative diseases:** CHCHD2 and CHCHD10 are homologous proteins that share 54% identity in their amino acid sequences. Although they are highly similar, mutations in CHCHD2 have been linked to PD and other Lewy body diseases, while CHCHD10 mutations are associated with amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD). In collaboration with the David Kang Lab, we are investigating the similarities and differences between the pathological impacts of CHCHD2 and its homolog CHCHD10, the latter of which is mutated in both familial and sporadic cases of FTD and ALS. (Relevant tools can be found in PMID: 28585542, 35787294, 38132101)
- **Sex differences in neurodegenerative diseases:** Alzheimer's disease (AD) affects women approximately 1.7 times more frequently than men, a disparity potentially linked to higher tau burdens in women even before symptoms manifest. Our recent publication in *Cell*, titled "X-linked Ubiquitin-Specific Peptidase 11 Increases Tauopathy Vulnerability in Women" (PMID: 36198316), demonstrates that USP11 promotes tau acetylation and aggregation through initiating tau deubiquitination. In collaboration with Dr. David Kang, we are developing and testing a series of neuroprotective USP11 inhibitors.

B. Techniques of interest: iPSC, STED microscope, In vivo 2P neuroimaging

Da Yong Lee, Ph.D.

Rare Disease Research center,
Korea Research Institute of Bioscience and
Biotechnology, Korea



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2014. 03. – up to now. Associate Professor, KRIBB School, Korea University of Science and Technology (UST), Daejeon, South Korea
2013. 11. – up to now. Senior Researcher, Rare Disease Research Center, Korea Research Institute of Bioscience and Biotechnology (KRIBB), Daejeon, Korea
2006. 09. – 2012. 09. Postdoctoral fellow, Washington University School of Medicine, St. Louis, MO, USA.
2001. 03. – 2005. 02. PhD, Neuroscience program, Ajou University, Suwon, Korea

Selected Publications:

1. Jeong B, Kim JS, Kwon AR, Lee J, Park S, Koo J, Lee WS, Baek JY, Shin WH, Lee J-S, Jeong J, Kim WK, Jung CR, Kim NS, Cho SH, Lee DY. Maternal nanoplastic ingestion induces an increase in offspring body weight through altered lipid species and microbiota. *Environ Int* **2024**, *185*, 108522. (IF 11.8)
2. Nam E, Lin Y, Park J, Do H, Han J, Jeong B, Park S, Lee DY, Kim M, Han J, Baik MH, Lee YH, Lim MH. APP-C31: An Intracellular Promoter of Both Metal-Free and Metal-Bound Amyloid- β_{40} Aggregation and Toxicity in Alzheimer's Disease. *Adv Sci (Weinh)*. **2024 Jan**;11(4):e2307182. (IF 15.1)
3. Lim JH, Kang HM, Kim DH, Jeong B, Lee DY, Lee JR, Baek JY, Cho HS, Son MY, Kim DS, Kim NS, Jung CR. ARL6IP1 gene delivery reduces neuroinflammation and neurodegenerative pathology in hereditary spastic paraplegia model. *J Exp Med*. **2024 Jan 1**;221(1):e20230367. (IF 15.3)
4. Jeong B, Baek JY, Koo J, Park S, Ryu YK, Kim KS, Zhang S, Chung C, Dogan R, Choi HS, Um D, Kim TK, Lee WS, Jeong J, Shin WH, Lee JR, Nam-Soon Kim, and Lee DY. Maternal exposure to PSNP causes the dysregulation of brain functions in progeny. *J Hazard Mater*. **2022**. *426*:127815 (IF 13.6).
5. Koo J, Park S, Sung SE, Lee J, Kim DS, Lee J, Lee JR, Kim NS, Lee DY. Altered Gene Expression Profiles in Neural Stem Cells Derived from Duchenne Muscular Dystrophy Patients with Intellectual Disability. *Exp Neurobiol*. **2021**. *30*(4):263-74.



Association of Korean Neuroscientists



Dr. Daewoo Lee

Professor

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Lab website: <https://www.ohio.edu/cas/leed1>

A. Research Focus and established techniques: Our research endeavors focus on unraveling the molecular and cellular mechanisms that underlie synaptic modulation and neurodegeneration. Our investigations are structured around three core projects:

- **Biogenic Amine Signaling and Olfactory Learning:** This project aims to elucidate the functional roles of dopamine (DA) and serotonin receptors in synaptic plasticity and olfactory learning. Of particular interest is the modulation of excitability and synaptic transmission underlying olfactory learning by D2 autoreceptors.
- **Cell-to-Cell Propagation of α -Synuclein:** The abundant neuronal protein α -Synuclein (α -Syn) can become pathogenic, leading to the formation of abnormal protein aggregates known as Lewy bodies (LBs) and contributing to neurodegenerative diseases like Lewy body dementia and Parkinson's disease. Our focus is on understanding the prion-like spreading of α -Syn, specifically investigating the impact of neuronal subtype, α -Syn alleles (wildtype vs. mutants), and various functional and molecular factors on its pathological transmission.
- **Mechanisms Underlying Activity-Dependent Human Tau Release:** Hyper-phosphorylated tau has been implicated in the spread of tau pathology throughout the brain in Alzheimer's disease. Studies suggest that tau can be transferred between synaptically connected neurons, with neuronal excitability playing a significant role in this process. Our research aims to uncover the genetic factors mediating activity-dependent tau release. By employing protein interactome approaches, we seek to identify proteins interacting with tau and elucidate their functional roles in the activity-dependent release of tau.
- **Established techniques:** Electrophysiology (patch clamp, amperometry), *Drosophila* and rodent primary neuronal culture, Human neuroprogenitor cell line (ReNCell), Cellular imaging/analysis, Western blot, ELISA, Confocal microscopy, Optogenetics & chemogenetics, *Drosophila* genetics (mutant & transgenic approaches), Behavioral assays (learning & locomotion)

B. Techniques of interest: Protein Interactome, NGS/RNA-Seq, Imaging



Association of Korean Neuroscientists



Dr. David Kang

Howard T. Karsner Professor in Pathology
Department of Pathology at Case Western Reserve University
Research Neurobiologist (GS-14)
Louis Stokes Cleveland VA Medical Center.

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Lab website: <https://www.kang-lab.com/>

A. Research Focus and established techniques: Unraveling the molecular mechanisms driving and opposing neurodegeneration associated with Alzheimer's disease (AD), traumatic brain injury (TBI), Frontotemporal dementia (FTD), Amyotrophic Lateral Sclerosis (ALS), neuromuscular disorders, and Lewy body diseases (LBDs).

- **Gender disparities in Neurodegenerative Diseases:** Alzheimer's disease (AD) is 1.7 times more prevalent in women than in men, potentially due to higher accumulations of tau proteins in women prior to symptom onset. Our recent article in *Cell*, titled "X-linked Ubiquitin-Specific Peptidase 11 Increases Tauopathy Vulnerability in Women" (PMID: 36198316), demonstrates that USP11 promotes the acetylation and aggregation of tau by initiating their deubiquitination. In collaboration with Dr. Alexa Woo, we are advancing the development and evaluation of various USP11 inhibitors.
- **Dissecting the Role of Slingshot Homolog-1 (SSH1) in AD Pathogenesis:** Over the past decade, my lab has been exploring the role of the Slingshot homolog-1 (SSH1) pathway in AD pathogenesis. SSH1, a multifunctional actin-binding protein with phosphatase activity on cofilin, is essential for A β 42-induced mitochondrial dysfunction and synaptic loss. This represents a crucial link between A β and tau pathogenesis. (Relevant tools can be found at: PMID: 33044112, 36637427, 36092812)
- **Nexus between the SSH1 and Nrf2 Pathways in Neurodegeneration vs. Neuroprotection:** We recently discovered that SSH1 also functions as a 'molecular brake' in the neuroprotective Nrf2 signaling pathway, exacerbating AD pathogenesis. We hypothesize that the SSH1-Nrf2 nexus is a critical determinant affecting the balance between neurodegeneration and neuroprotection during proteotoxic and oxidative stress in AD and related diseases. By employing in vitro and in vivo models, along with biochemical, molecular, single nuclear RNA-sequencing, and proteomics tools, and examining postmortem human brains, we are dissecting the SSH1-Nrf2 nexus to understand its regulation both physiologically and pathologically. We have identified several SSH1 inhibitor compounds with potential therapeutic benefits for AD and other brain injuries. Our goal is to use these inhibitors in conjunction with brain-targeted nanoparticle strategies to enhance autophagy, reduce mitochondrial dysfunction, and promote neuroprotective Nrf2 signaling. (Relevant tools can be found at: PMID: 37463212, 36092812)
- **Pathological Signatures of CHCHD10 Dysfunction in ADRDs:** This project aims to elucidate the pathological signatures of CHCHD10-driven pathogenesis, assess the role of both wild-type and mutant CHCHD10 in mitigating pathological phenotypes, and identify therapeutic targets to improve patient outcomes. (Relevant tools can be found at: PMID: 28585542, 35787294, 38132101)

B. Techniques of interest: Deep learning, spatial transcriptomics, STED microscopy, single-cell proteomics, multi-electrode array Ephys, TMS, TES



Association of Korean Neuroscientists



Dr. Dongjoo Choi

Instructor

Center for Cancer Neuroscience at Baylor College of Medicine
Center for Cell and Gene Therapy at Baylor College of Medicine

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A. Research Focus and established techniques:

1. Functional alteration of glial cells in the injured brain and neurodegenerative diseases (AD and PD).

My primary research objective in this area is to elucidate the role of astrocytes in the brain within the aging and the pathological conditions.

(Tools can be found at : <https://www.ncbi.nlm.nih.gov/myncbi/collections/mybibliography/>)

Current project and interest

A. The functional alteration of astrocytes in the initiation and progression of AD: My research focuses on key mechanistic pathways of astrocytic specific transcription factor for Amyloid-beta metabolism and clearance system in AD-associated astrocyte.

B. The functional alteration of astrocytes in the aged brain: My research focuses on the aging-mechanisms associated with astrocytes specific transcription factors in astrocytes and correlation between astrocytes and neuron in the aged brain.

2. The initiation and progression of Brain cancer (glioma).

My overarching research goal in this part is to identify the novel insight, mechanism, and target that regulates the initiation and progression of GBM and develop therapeutic strategies.

Current project and interest

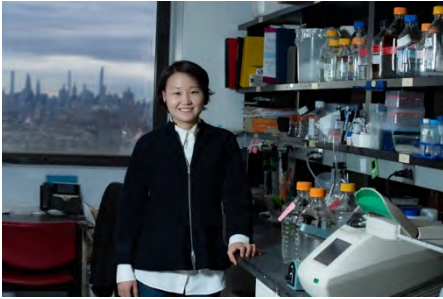
A. The initiation and progression of aggressive glioma: My research focuses on the identifying the new tumor suppressor genes that contribute to Familial Gliomas by In vivo Barcode screening.

B. Identifying novel GSCs marker and functional mechanism: My research focuses on the identifying a specific target regulated in aggressive glioma tumors, with enrichment observed in mouse and human glioma stem cell (GSC) populations.

B. Techniques of interest: fMRI, PET imaging, Electrophysiology



Association of Korean Neuroscientists



Dr. Hachung Chung

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A. Research Focus and established techniques: My scientific training has been rooted in immunology, but recently our team has been venturing into neurobiology. I received my B.S. degree from Stony Brook University, where I worked on host-bacterial interactions as an undergraduate researcher. For my graduate studies (Harvard University), I colonized germ-free mice with mouse or human microbiota, and discovered that the mammalian gut requires 'host-specific' bacterial species for proper immune maturation (Chung et al. *Cell* 2012). For my post-doctoral studies (The Rockefeller University), I demonstrated that the RNA editing enzyme ADAR1 is required for self vs. non-self RNA differentiation by our innate immune system (Chung et al. *Cell* 2018). I started my independent laboratory at Columbia University in 2019. Our team studies neurodegeneration through the lens of an immunologist. We are investigating if autoinflammatory reactions against endogenous (self)-RNAs is an early event that initiates and accelerates neurodegeneration. By imaging double-stranded RNAs (dsRNAs) in various human cell types, including human neurons differentiated from stem cells, we discovered that human neurons express exceptionally high levels of immunostimulatory dsRNA structures that constantly induce a low level of inflammation (Dorrity and Shin et al. *Science Immunology*, 2023). These findings hint that immunity and neuronal function are deeply intertwined.

B. Techniques of interest: hESC and iPSC differentiation to neural lineages, modeling neurodegeneration, dsRNA sequencing methods, profiling innate immune responses etc.



Association of Korean Neuroscientists



Dr. Hyewhon Rhim

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Lab website: <https://kist.re.kr/fcsc/index.do>

A. Research Focus and established techniques: *O-GluNacylated protein modification, Serotonin receptors, Depression, Alzheimer's diseases, Natural Compounds(Ginsenosides, Gintonin), Policies in Convergence Research and Women Scientists*

- ***O-GluNacylated protein modification.*** Our research focuses on the mechanisms associated with a reversible, dynamic and highly abundant post-translational modification, *O-GluNacylation, in brain using OGA+/- heterozygous transgenic mouse* (Tools can be found at: PMID: 32332789, 31827688, 31086206, 29223644, 28368052).
- ***Serotonin receptors and its binding proteins.*** Among 7 different subtypes of serotonin receptors, our research focuses on mechanisms of serotonin receptor 6 and its binding proteins in brain (Tools can be found at: PMID: 30853821, 30028132, 28681593, 26852005, 24614691, 20093369)
- ***Natural compounds(Ginsenosides, Gintonin).*** Our research is dedicated to explore beneficial effects of natural compounds, ginsenosides and gintonin, in various neurodegenerative disease models and identify the mechanisms for therapeutic applications (Tools can be found at: PMID: 38223830, 32372871, 32148391, 30337800, 27765516, 18078425)

B. Techniques of interest: brain-slice physiological measurements, calcium imaging, protein-binding related tools



Association of Korean Neuroscientists



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Lab website: <https://www.hkleelab.org>

A. Research Focus and established techniques: *Developmental gliogenesis and associated disorders; white matter injuries (PVL, HIE, MS), brain cancer (GBM), stroke, vascular dementia, neuropsychiatric diseases.*

- **Myelin development and regeneration (white matter injury).** Our research focuses on the mechanisms associated with Wnt signaling in myelin development and regeneration, and pinpoint potential targetable pathways for white matter disorder (Tools can be found at: PMID: 25754822, 32792353, 35101966, 37084732, 37607236)
- **Astrocyte development and reactivity (ischemic stroke).** Our research focuses on key mechanistic pathways by which astrocytes govern blood-brain barrier recovery after ischemic stroke. We hope our research can lead to discovery of novel glia-specific therapeutic approaches, such as astrocytic metabolism-cytokine coupling, to stimulate brain repair after stroke injury (Tools can be found at: PMID: 34633730, 31498149, bioRxiv 2023.04.03.535167)
- **Brain cancer, glioblastoma.** Our research is dedicated to exploring the mechanisms at play between glioma and the tumor microenvironment, with a goal to identify novel, actionable pathways for therapeutic intervention. (Tools can be found at: PMID: 29053101, 28166219, 28892058)

B. Techniques of interest: In vivo 2P/3P neuroimaging, Human MRI, pH sensors, physiological measurements



Association of Korean Neuroscientists



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A. Research Focus and established techniques:

Neuropharmacology of Alcohol Use Disorders and Psychiatric Disorders. The main goal of our research is to investigate brain glutamate signaling in alcoholism and psychiatric disorders by using a behavioral neuroscience approach. Interestingly, both genetic and environmental factors contribute to alcoholism, influencing susceptibility and treatment responsiveness. Thus, we believe that linking addictive behaviors with a glutamate neuromodulation process and also intracellular calcium mechanisms is essential to understanding psychiatric symptoms and how to treat them better. The focus of our research is to elucidate the neurogranin (Ng) mechanism that underlines relevant addictive behavioral phenotypes in rodent models using a combination of cutting-edge techniques in the areas of mouse genetics, neuroproteomics, neuropharmacology, and behavioral neuroscience.

Neurogranin-mediated Endothelial Activation. We study the endothelial nitric oxide synthetase (NOS) mechanism using calcium-dependent neurogranin (Ng) signaling. Ng expression in the brain attenuates calcium-CaM complex formation and is critical in regulating neuronal nitric oxide synthase (nNOS) activation. Our recent study identified that Ng is also expressed in endothelial cells and plays an essential role in endothelial nitric oxide synthase (eNOS) activity. Consistently, our new results indicate that Ng expression is significantly decreased in the left anterior descending artery of coronary artery disease patients. We therefore hypothesize that Ng dysregulation expression decreases NO bioavailability resulting in endothelial activation and inflammation, thus contributing to the promotion of atherosclerosis. We have used both in vitro and in vivo model systems using a combination of cutting-edge techniques, including CRISPR/Cas9, flow-mediated dilation, partial carotid ligation, and label-free proteomics. Overall, our studies will have a broad impact on the field by dissecting the crucial roles of Ng-mediated eNOS regulation in regulating endothelial activation.

Pharmacometabolomics and Pharmacoproteomics for Alcohol Use Disorder. We have studied drug efficacy biomarker studies using metabolomics and proteomics to elucidate pharmacological intervention in alcohol use disorders. We have examined blood metabolite, or brain tissue protein changes as a result of medication treatment and has found a possible metabolism in alcoholism patients that is associated with a positive outcome of medication treatment. We believe that our research will help to identify the best treatment option for a specific sub-population and contribute to the development of drug efficacy biomarkers for personalized medicine in alcohol use disorders.

B. Techniques of interest: Neuroproteomics, Phamacometabolomics, Behavioral Neuroscience, Mouse Genetics, Neuropharmacology.



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A. Research Interests

Our long-term focus is to explore the role of lipids in non-neuronal cells and their contribution to neurodegeneration, with a particular emphasis on neuroinflammation. Currently, we are investigating the importance of preserving sphingolipids balance within the nervous system, a key element in preventing neurodegeneration and synaptic dysfunction. Our recent studies on *Drosophila* have revealed the combined effect of increased levels of Ceramides and sphingosine-1-phosphate (S1P) in glia and hemocytes (fly immune cells). These increased levels trigger the activation of the NF- κ B pathway within the nervous system, an event that precedes cell death. We are keen to further explore these lipids within glia and hemocytes, hoping to uncover the molecular mechanisms behind various neurodegenerative diseases. Using flies for initial variant assessments, we aim to uncover lipid metabolic genes not yet associated with human disease. Our methods encompass several fly-based strategies to evaluate variant function and gain a deeper understanding of these genes, including humanization strategies facilitated by CRISPR-Cas9. High-priority genes without existing mouse models will be targeted for mouse knockout generation and phenotyping, and human cells will be used to confirm findings when possible and appropriate.

B. Research Projects and established techniques

Investigate the cell-autonomous roles of S1P in glia. High S1P production by glial cells robustly activates NF- κ B pathway signaling. However, the precise mechanism by which S1P activates NF- κ B and the full repertoire of S1P-mediated signaling in glia remain unclear. We will employ single-cell sequencing (scRNA-seq) in flies expressing variable levels of S1P to comprehensively characterize the signaling events downstream of S1P, including NF- κ B, in fly brains. Furthermore, we will validate these signaling events in *in vitro* model systems and in human postmortem material.

***Drosophila* Functional core for human disease studies.**

Flies are an ideal system for initial variant assessment, given that the enrichment of conserved-disease genes is about 80%, and studies using fruit flies have successfully identified new human disease genes. Many patients with rare diseases have been undiagnosed for many years. This 'diagnostic odyssey' severely impacts the lives and quality of life of patients and their family members and is costly for our society. Collaborating with clinical geneticists, we facilitate disease diagnosis by performing functional studies of candidate genetic variants identified through whole-exome and whole-genome sequencing techniques. We further dissect the underlying disease mechanisms and explore the therapeutic options via FDA-approved drug screening. We use multiple strategies in flies to assess variant function and a deeper mechanistic understanding of these genes. These include humanization strategies by replacement of the fly gene by human reference or variant cDNA facilitated by CRISPR-Cas9.

C. Techniques of interest

CRISPR-Cas9, scSeq, Lipidomics, electroretinogram, WGS/WES, Transgenesis



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A. Research Interest

My lab currently focuses on understanding the role of innate immune cells in the progression of Lewy body disorders including Parkinson's disease (PD). We utilize a combination of *in vivo* and *in vitro* models of synucleinopathies to uncover the interaction between innate immune cells and abnormal protein aggregates. The long-term goal is to explain how the immune system influences PD-associated brain changes, which may represent a novel mechanism and an avenue for treating neurodegenerative diseases.

B. Research Project and established techniques

We utilize a combination of *in vivo* and *in vitro* models of synucleinopathies to uncover the interaction between innate immune cells and abnormal protein aggregates. We have established the mouse model of Lewy body diseases that exhibits many clinically relevant hallmarks of PD including dopaminergic cell loss, behavior deficits, and synucleinopathies. By utilizing this mouse model, we conducted a complete characterization of immune cell composition during a prodromal stage of the disease to determine whether CNS-initiated α -synucleinopathies alter immune cell profiles in the CNS and the periphery.

Innate immune lymphocyte in Lewy body diseases. My lab investigate the role of natural killer (NK) cells in the context of Parkinson's disease (PD). For that, I have established the relevant *in vivo* animal model, preformed fibril (PFF) alpha-synuclein (α -syn)-induced PD mice, which exhibit many clinically relevant hallmarks of PD including dopaminergic cell loss, behavior deficits, and synucleinopathies. By utilizing this model, I propose to investigate whether NK cells are neuroprotective or neurotoxic in PD. Both *in vitro* studies demonstrated that human NK cells efficiently clear extracellular α -syn and the systemic depletion of NK cells resulted in the exacerbated disease phenotypes in synucleinopathies *in vivo* (Earls et al, PNAS 2020). Based on these data, I hypothesized that NK cells play a neuroprotective role against synuclein pathology and neurodegeneration. Currently, we investigate the precise mechanism(s) by which NK cells reduce α -synuclein burden, modulate inflammation, and exert neuroprotection.

Modulating Microglia in Lewy body diseases. Our research program is to determine the extent to which microglia contributes the onset and/or progression of neurodegenerative diseases. Age-related changes in inflammation and metabolism in peripheral tissues and the brain have been implicated as risk factors for neurodegenerative diseases. However, the detailed mechanisms of how age-related inflammation and associated-metabolic changes affect the onset and/or progression of neurodegeneration have not been elucidated. Previously, I have identified a novel regulator of microglia activation and neuroinflammation, Regulator of G-protein Signaling (RGS) 10, and its neuroprotective effect on the nigrostriatal pathway. We generate microglia-targeting nanotherapeutics carrying RGS10 plasmid and AAV-mediated RGS10 gene delivery to attenuate pathology utilizing PFF α -syn-induced mouse model of Lewy body disorders. Our goal is by enriching RGS10 in microglia, we restores microglia homeostasis, enhances amyloid fibril clearance, therefore exerts neuroprotection for amyloid fibril-induced neuronal death as a potential therapeutics.

C. Techniques of Interest

Single cell analysis, Proteomics, Metabolomics



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A. Research Focus and established techniques

Neural representation of motor planning in dynamical motor system: The major goal of my research program aims to understand the neural underpinnings of the long-term maintenance of diverse motor skill repertoires. Specifically, I investigate the stability and flexibility of preparatory activity for movement in the face of continual learning. If we execute the same learned action today and 1 year later, does the neural representation for motor planning remain consistent? Furthermore, if we subsequently learn different motor skills, these learning experiences may alter existing representation of motor preparation? I study these problems in mice using directional licking as a model for learned actions. I utilize automated home-cage training system to establish continual learning paradigm in which mice learn to perform directional licking in different behavior tasks. Combining this behavior paradigm with longitudinal two-photon calcium imaging, I monitor the activity of motor cortex activity over a period of up to 6 months.

Relationship between functional and genetic cell-types: The second goal of my research program is elucidating a relationship between functional and genetic profiles. My preliminary results reveal the presence of specialized functional cell-types in mouse motor cortex showing consistent activity patterns across different behavior tasks. Then, what factors make each functional cell-type special and exhibit a unique activity profile? I hypothesize that distinct transcriptomic expressions may give rise to different functional cell-types with unique activity profiles. To study this problem, I will use CaMPARI system to tag a group of neurons showing a specific activity pattern by shining a light when they are active and subsequently perform single-cell RNA sequencing from individual functional cell-types. In this way, I want to discover genetic markers, which potentially enable to induce a particular activity pattern from each functional cell-type.

B. Techniques of interest

Automated home-cage behavior training system, *in vivo* two-photon calcium imaging and Neuropixels recording from task performing mice, large-scale neuronal population analysis using dimensionality reduction and decoding approaches, computational modeling with recurrent neural network, tagging active neurons using light, single cell RNAseq.



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A. Research Focus and established techniques: *Mood disorders (depression, PTSD), psychiatric diseases (schizophrenia, autism spectrum disorders).*

- **Social stress and habenula function.** Our research focuses on how early adversity affects later-life cognitive function. We established early life stress animal models such as social isolation and maternal separation to investigate the synaptic and behavioral alteration in brain regions including the habenula, amygdala, and hippocampal CA2 region, particularly. (Tools can be found at: PMID: 37771409, 36351843, 23974710, 18165656)
- **Astrocytic dysfunction and brain disease .** Our research focuses on key mechanistic pathways by which astrocytic dysfunction such as aberrant gliotransmitters via reactive astrocytes, is involved in neurodegenerative disease and psychiatric disorders. We hope our research can lead to the discovery of novel glia-specific therapeutic approaches for brain diseases including Parkinson's disease and depression. (Tools can be found at: PMID: 31928877, 30906861)
- **Neuromodulation.** Our collaborative research is actively being pursued to reveal underlying mechanisms of non-invasive neuromodulation to identify novel, actionable pathways for therapeutic intervention, which provide improvement of cognitive function and overcoming brain disorders. (Tools can be found at: PMID: 36259285, 33450428, 31439845)

B. Techniques of interest: In vivo calcium imaging, spatial transcriptomics, physiological measurements



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A. Research Focus:

- **Neurobiological mechanisms of acute pain.** My earlier work during the postdoctoral and junior faculty period was directed toward neurobiological mechanisms of acute pain. These include the characterization of nociceptors, spinothalamic tract neurons in the non-human primate, and the spinal and thalamic neuronal circuitry involved in pain sensory function.
- **Development of an animal model for chronic pain (neuropathic pain).** I developed an animal model for neuropathic pain, known as the segmental spinal nerve ligation (SNL) model (nickname – the Chung model). This model became very popular and two papers related to the model development received more than 12,500 combined citations as of April, 2024. We study how the processing of pain sensory signals is normally modulated at the supraspinal level and whether this processing is compromised in neurodegenerative diseases.
- **Investigation of various mechanisms underlying chronic neuropathic pain.** We found several critical factors involved in development of neuropathic pain. These include: 1) abnormal ectopic discharges, 2) sympathetic sprouting, 3) sodium channel upregulation, and 4) genetic factors.
- **Reactive oxygen species (ROS) involvement in neuropathic pain.** We found that ROS are critically important as intracellular signals activating various downstream kinases to produce synaptic plasticity and sensitization of neurons in the spinal cord in a neuronal type specific manner.

B. Contribution to AKN:

- **AKN founding member (1 of 8)** – in 1982
- **AKN Secretary for initial 14 years** – Wrote AKN Initial Bylaw in 1988.
- **AKN President for 3 terms (6 years)** – 1) Created AKN Student Research Awards in 1996, 2) Adopted AKN Logo in 2009, 3) Created AKN Junior Faculty Awards in 2011.



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Dr. Juhyun Kim

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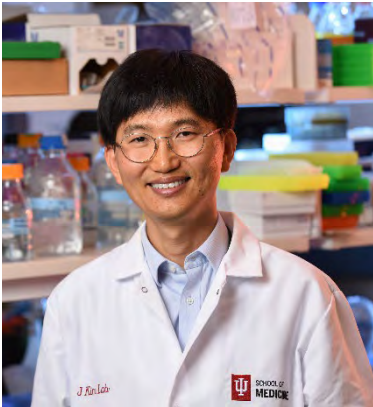
A. Research Focus and established techniques: *Neurophysiological mechanisms underlying cognition, affection, and behaviors in normal brains and mental disorders.*

- **Cortical circuit alterations in psychiatric and neurodevelopmental disorders.** Abnormalities in the synaptic organization of excitatory and inhibitory neurons and their activities have been identified in various brain disorders. We are interested in the circuit mechanisms responsible for excitatory/inhibitory (E/I) circuit dysfunctions and behavioral abnormalities observed in mental disorders including autism-spectrum disorders, depression, anxiety, and PTSD
- **Neural mechanisms of the pathology of drug addiction and the physiology of psychedelics.** We study whether and how the cortical and subcortical structures change their cellular function and circuit dynamics in drug addiction or psychedelic treatment.
- **Cellular and synaptic mechanisms controlling sexual behaviors.** We aim to study physiology and pathology of the rewarding circuits responsible for normal sexual behaviors and compulsive/addictive sexual behaviors.

B. Techniques of interest: In vitro whole-cell patch-clamp electrophysiology, addiction behaviors



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A. Research Focus and established techniques:

Research Focus: *Alzheimer's disease, Alzheimer's disease related dementia, Lipid metabolism, Regulation of transcriptome by microRNAs and transcription factors, Role of cytoskeleton proteins in neuroimmune function, Drug discovery (small molecules and biologics)*

Established techniques: *Single cell & nucleus RNA-seq, Spatial transcriptomics, Proteomics, Magnetic resonance imaging, iPSC, Quantitative trait loci mapping, Adeno-associated viruse (AAV)-based disease modeling, Antisense oligonucleotides- and AAV-based preclinical trials*

B. Techniques of interest: *Spatial proteomics, Single cell proteomics, CRISPR screening, Multi-electrode array*



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Dr. Jun Hee Kim

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A. Research Interest : The core objective of Dr. Kim's research program is to elucidate the mechanisms regulating synaptic function and dysfunction, particularly in the context of CNS myelination during the development of the auditory nervous system. Expanding the scope of research, Dr. Kim's team also probes the dynamic communication between neurons and glia in the brain. By leveraging cutting-edge electrophysiological and imaging techniques, the program endeavors to reveal the neurophysiological underpinnings of central auditory dysfunctions. The overarching aim of our research is to bolster both preventive and therapeutic strategies for auditory disorders. These disorders can arise from various neurodevelopmental conditions, such as Autism Spectrum Disorder (ASD), or from neurodegenerative diseases like Alzheimer's Disease. A deep and nuanced understanding of the mechanisms at play could lead to substantial improvements in the quality of life for innumerable individuals affected by these debilitating conditions.

- Synaptic transmission and plasticity
- Oligodendroglia physiology and myelination
- Neuron-glia communication
- Auditory neuroscience

B. Techniques of interest: Major techniques used in the lab

- In vivo and ex vivo electrophysiology
- Single-cell imaging: Ca²⁺ imaging
- Patch-clamp recording combined with single-cell sequencing: Patch-seq
- Animal behaviors related to auditory functions



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A. Research Focus and established techniques:

- **Understanding spinal mechanisms of pain chronification.** Focusing on long-term changes in sensory neuronal circuits (including their interactions with glial cells) at the spinal level, we study how an injury-induced acute pain becomes chronic, persisting beyond its normal resolution time.
- **Understanding supraspinal pain modulatory mechanisms.** We study how the processing of pain signals is normally modulated at the supraspinal level and whether this processing is compromised in chronic pain conditions and neurodegenerative diseases.
- **Development of novel pain therapeutics.** Teaming up with experts in medicinal chemistry, high-throughput screening using cell-based assay systems, and pharmacokinetics, we discover and develop novel pain therapeutics with little to no abuse liability.
- **Established techniques.** We model various pain conditions in animals (e.g., neuropathic pain due to peripheral neuropathy, post-surgical pain, nociplastic pain due to abnormal prolongation of acute injury-induced pain, etc.) and identify molecules/neurons/circuits that underlie the pain conditions and/or mediate pain therapeutics' effects using behavioral, histological, molecular biological, and imaging (*ex vivo* slice imaging and fiber photometry) approaches.

B. Techniques of interest: (single-cell) RNA-seq analysis, whole brain imaging after optical clearing, machine learning-based automation of data analysis, genome-wide association studies (GWAS)



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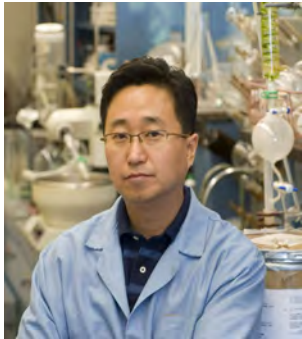
A. Research Focus and established techniques: *Neural dynamics of learning and memory underlying decision-making; Brain-wide functions of neuromodulators; Functional neural circuit mapping tool development.*

- **Dopamine-mediated neural dynamics.** Dopamine is an important neuromodulator involved in the brain's reward system and learning and memory. Our work explores how dopamine influences neural activity and drives behavior under uncertainty. Determining the specific role of dopamine in neural encoding is necessary to understand how dopamine controls behaviors during health and disease. (<http://dx.doi.org/10.2139/ssrn.3630322>, PMID: 33951422)
- **Neural mechanisms of foraging decision-making.** Our research investigates the brain processing behind efficient actions during foraging decisions. Along with a computational model based on reinforcement learning, behavioral experiments in rats and rhesus monkeys revealed how decision dynamics emerge from the interaction of efficient habitual and goal-directed systems. Our studies identify neural substrates for the dynamics and provide distinct computational mechanisms for the timing and content of foraging decisions, involving state control and goal-directed and habitual control (PMID: 24376758, 25122498, 28992274, 31354461)
- **Development of technologies for spatio-temporally precise mapping of functional neural circuits.** Identifying and manipulating functionally-defined neural circuits are critical to understand how the brain operates for specific behaviors. Our research focuses on development of novel techniques with a newly designed gene expression system that allows researchers to visualize and manipulate functional neural circuits (PMID: 28369042, 28650460, 30643148, 37730989, 38191933)
- **An adaptive behavioral control motif mediated by cortical axo-axonic inhibition.** Our research focused on the Chandelier cell (ChC), a specific type of inhibitory interneuron known for its unique features such as GABAergic properties and fast-spiking electrophysiology. We discovered that ChCs establish cortical microcircuits, enabling real-time neural coding through selective axo-axonic synaptic plasticity (PMID: 37474640, 36299494)

B. Techniques of interest: in vivo electrophysiological recording, in vivo two-photon microscopy for calcium and biosensor imaging, miniature microscopy with optogenetic manipulation, dual-color fiber photometry recording, computational neuroscience of animal behavior with deep reinforcement learning



Association of Korean Neuroscientists



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A. Research Focus and Established Techniques: My long-term goal is to integrate nanotechnologies and chemical biology tools to modulate CNS injuries/diseases and control stem cell/immune cell fate and behaviors effectively and selectively. To address challenges in conventional stem/cancer cell biology, my Rutgers research program focuses on developing novel methods such as nanoparticle-based drug/gene delivery, molecular imaging, nanobioscaffolds, and microfluidics to investigate and modulate complex signaling pathways controlling cell behaviors.

A.1. Promoting Axonal Regeneration in the injured CNS using a Non-viral Gene Manipulation method:

The CNS has limited regenerative potential and a complex inhibitory environment. This project integrates nanotechnology, biomaterials, chemical biology, neuroscience, and stem cell biology to develop a novel nanomaterial-based platform. The platform aims to induce safe, effective, and innovative axon regeneration and neurite outgrowth for in vivo transplantation and potential clinical applications.

A.2. Advanced Stem Cell Therapies for CNS injuries and Advanced in vivo Drug/Gene Delivery using Bioinspired Hybrid Nanoscaffolds:

Stem cell transplantation for CNS diseases faces challenges like low cell survival, incomplete differentiation, and limited neurite outgrowth in vivo. We developed a biodegradable hybrid inorganic (BHI) nanoscaffold to improve human neural stem cell (NSC) transplantation and control differentiation. Biomaterials for CNS tissue engineering aim to provide favorable microenvironments for cellular regeneration and serve as controlled drug release platforms. Our nanoscaffold technology can be combined with developing neurogenic drugs and stem cell therapies.

A.3. Transforming Theragnostics in Neurological Diseases using NanoBiotechnology-based Liquid Biopsy:

Liquid biopsy advancements have expanded its application to neurodegenerative diseases, providing a less invasive diagnostic, prognostic, and therapeutic tool by analyzing biological fluids for molecular biomarkers. Focusing on blood and CSF enables continuous CNS monitoring for changes indicative of Alzheimer's, Parkinson's, and ALS. Extracellular vesicles (EVs) reflect cellular states and can cross the blood-brain barrier, allowing the detection of CNS-derived biomarkers in peripheral blood. Our research pioneers a nanotechnology-enhanced liquid biopsy platform integrating CRISPR-based biosensing to isolate disease-specific EV miRNAs, offering a novel, sensitive method for early diagnosis of neurodegenerative conditions.

A.4. Multifunctional Nanoparticle-Assisted Non-Viral CRISPR-Cas9 for Advanced Genome Editing:

CRISPR-Cas9 has the potential to revolutionize disease treatment, including neurological disorders, by correcting genes or mutations in human patient cells. However, challenges such as low delivery efficiencies, genome-editing efficiency, and precision need to be addressed before widespread clinical application. We have developed a Magnetic Nanoparticle-Assisted Genome Editing (MAGE) platform that improves the transfection efficiency, biocompatibility, and genome-editing accuracy of CRISPR-Cas9. This nanobio-combined CRISPR-Cas9 technology offers potential for various clinical applications, particularly in stem cell therapies targeting genetic diseases.

B. Collaboration Interest: Neurodegeneration/Neurological Disorders with Animal Models and Human Samples.



Association of Korean Neuroscientists



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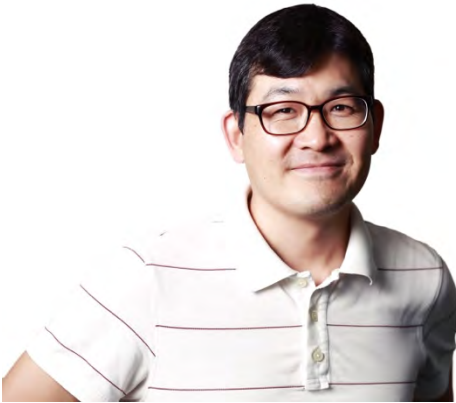
A. Research Focus and established techniques:

- Neuromodulatory mechanism underlying behavioral control and plasticity
- Dopamine, octopamine, acetylcholine
- Learning, memory, inhibitory control, impulsivity, disinhibition, courtship, ovulation
- Autism spectrum disorder, addiction (alcohol), dementia (ADRD)
- *Drosophila melanogaster*
- Genetic manipulations of genes, molecular functions, neuronal activities and neural circuits
- Fly behaviors (e.g. classical and operant conditioning, Go/No-Go test, flypub, flytracker, sleep, etc.)
- Immunohistochemistry, confocal microscopy, imaging, molecular analyses

B. Techniques of interest: *in vivo* fly brain imaging, omics, single-cell RNAseq, GWAS on human subjects



Association of Korean Neuroscientists



Dr. Mean-Hwan Kim (김민환)

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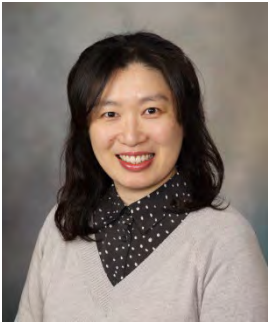
A. Research Focus and established techniques: *Cortical circuits organization; Development of synaptic transmission; Neuromodulatory effects on cortical computation; Circuit organization between species (translational approach).*

- **Local and long-range synaptic connectivity in cortical circuits.** Our research focuses on the mechanistic understanding of mammalian neocortical circuits organization and their functional roles (Tools and Research can be found at: PMID: 30415996, 38244539).
- **Neuromodulatory effects on intrinsic membrane properties, and synaptic transmission in cortical circuits.** Our research focuses on neuromodulatory effect on intrinsic membrane properties of individual neurons and their synaptic transmission by neuromodulators such as serotonin, adenosine, norepinephrine, etc.
- **Circuits organization between species (evolutionary perspective).** Our research is dedicated to explore and characterize potential evolutionary conserved and divergent features of cellular properties of cortical neurons and their synaptic transmission among different mammalian species such as mouse, non-human primates, and human (Tools can be found at: PMID: 37249212, 34616067, 35271334).

B. Techniques of interest: *In vitro* slice patch-clamp electrophysiology, *In vivo* 2-photon calcium imaging, Computational modeling



Association of Korean Neuroscientists



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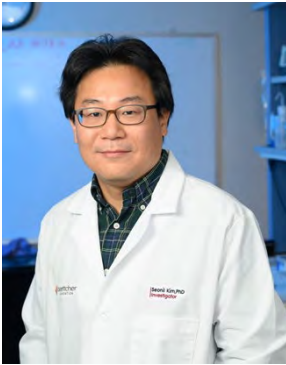
A. Research Focus and established techniques: *Neural stem cell development, Adult neurogenesis, Regenerative medicine, Chemobrain, Neurodevelopmental and Neurodegenerative disorders*

- **Adult neurogenesis as a regenerative strategy in neurodegeneration.** In Alzheimer's disease (AD), there is a notable decrease in Wnt signaling, which is believed to contribute to the development of the disease and the subsequent decline in memory. Consequently, activation of Wnt signaling may play a beneficial role in AD. While prior studies have focused mainly on Wnt downstream effectors to activate Wnt signaling, we aim to identify upstream targets capable of simultaneously activating multiple key Wnt downstream effectors and ultimately have far-reaching therapeutic potential.
- **Identification of juvenile protective factor (JPF) in brain aging:** Given the presence of juvenile protective factor (JPF), early postnatal development represents a period of robust plasticity and resistance/resilience which subsequently declines with aging. Diminution or disappearance of JPFs could contribute to the onset of age-related functional decline. We are particularly interested in discovering novel JPFs that are capable of rejuvenating neural plasticity and cognitive function in aged cohorts.
- **Developing druggable therapeutic targets for chemobrain:** Chemotherapy-induced cognitive impairment (also known as "chemobrain") is a neurotoxic side effect of chemotherapy that remains a significant medical challenge for cancer survivors, with no known cure. We aim to uncover the key molecular contributors driving chemobrain and develop rationally designed synergistic disease-modifying therapeutic strategies, thus ultimately improving the quality of life for cancer survivors.

B. Techniques of interest: Single-cell RNA-seq, Spatial Transcriptomics, Metabolomics, Proteomics, Drug Discovery, Brain drug delivery



Association of Korean Neuroscientists



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A. Research Focus and established techniques: Our lab researches synapse biology and neuron function and how synapse contributes to behavior in brain disorders. We study the changes in synapse structure and function in neurons. We focus on the signaling pathways and receptor trafficking mechanisms that control synaptic transmission and synapse strength. Many of our studies have been conducted in cultured neurons, a highly versatile system for analyzing synapse function. We also employ genetically modified mice to study brain function and diseases.

B. Techniques of interest: We extensively use techniques of cell biology, calcium imaging, biochemistry, and behavioral analysis, as well as in vitro and in vivo electrophysiology to deduce molecular mechanisms that control synapses and behavior.



Association of Korean Neuroscientists

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Dr. Yoo's research interest is to understand the function and mechanism of circadian clocks at levels from genes to behavior. In response to daily environmental changes imposed by Earth's rotation, almost all species, ranging from cyanobacteria to humans, have evolved physiological and behavioral rhythms, called circadian rhythms. The harmony between our intrinsic biological timing and the daily environmental oscillation is critical to physiological well-being; conversely, disrupted circadian rhythms have been shown to cause or increase the risk of various chronic diseases. Dr. Yoo's lab focus on delineating fundamental cellular mechanisms in circadian rhythms and also deciphering physiological and pathological roles of the clock. Dr. Yoo's long-term goal is to translate such fundamental mechanistic knowledge into new drug targets and therapeutic strategies for improved prevention and treatment of chronic diseases.



Association of Korean Neuroscientists



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A. Research Focus and established techniques: *Development, function, and dysfunction of ascending somatosensory pathways*

Functional organization of ascending somatosensory circuitry

The perception of touch and pain is multidimensional; upon touch or pinch of our skin, we discriminate between a gentle stroke and a sharp pinch, turn our body and head towards the stimuli, and evaluate hedonic values associated with them (pleasant vs. hurting). Moreover, how we perceive and react to different sensory cues is influenced by the nature of sensory stimuli; touching a hot pan and caressing a dog give rise to different sensations and behavioral responses. Our lab is interested in studying how ascending somatosensory circuitry endows us with this complex sensation of touch and pain and reaction to them.

Dysfunction of ascending somatosensory circuitry

Touch and pain are subjective experiences that are greatly modulated by internal states as well as pathological conditions: a gentle touch can be perceived as painful or disturbing in people with neuropathic pain or autism spectrum disorders. Our lab is interested in studying how disease states shape our sense of touch and pain and what molecular, cellular, and circuit mechanisms underlie the dysfunction of ascending somatosensory circuitry. This may reveal new therapeutic strategies for treating disorders associated with touch and pain.

Development of ascending somatosensory circuitry

Ascending spinal pathways consist of multiple independent modules that convey touch and pain signals to many different regions in the brain, including the brainstem, pons, midbrain, and thalamus. The sophisticated structural connectivity enables precise propagation of somatosensory signals from the periphery to the brain, underlying our sensation of and reaction to touch and pain. Our lab is interested in studying how these complex ascending somatosensory circuits are wired during development and what developmental programs control their formation and organization.

B. Techniques of interest: In vivo imaging/ephys, mouse genetics



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A. Research Focus and established techniques: *Sensory processing during navigation.*

Entering a room that we've never been inside before, we usually get our bearings within a few moments. In those moments, mammals like us are thought to create and update abstract internal representations of our surroundings. We are thought to then use these representations along with a sense of the current behavioral context to determine what actions to take next. Our lab is interested in understanding the brain-wide, multi-sensory information processing and integration that underlies this ability. To elucidate how the brain enables navigational decisions, we use a powerful genetic model organism, *Drosophila melanogaster*, which needs to solve some of the same navigational problems. Recent discoveries of compass-like neural representations in their brains suggest that they may even use some of the same tricks, which gives us the opportunity to understand these neural computations at the level of well-defined circuits, neurons and synapses. We combine a wide range of techniques including two-photon calcium imaging and electrophysiology in head-fixed behaving flies, cell-type specific optogenetic perturbation, electron-microscopy (EM) based neural circuit reconstruction, quantitative behavioral analysis of freely behaving flies and computational modeling of networks, to establish causal links from the neural circuit dynamics to cognitive behavior.

B. Techniques of interest

Two-photon imaging: We combine virtual reality and physiology. A tethered fly is allowed to walk on a ball or fly, while its behavior is monitored. We measure the rotation of the ball, or measure the difference between fly's left and right wingbeat amplitudes and use this motor information to let the fly control the rotational velocity of the visual environment. We call this a closed-loop experiment because we close the loop from the fly's motor output to the visual scene that the fly experiences. We express the genetically encoded calcium indicator, GCaMP, in a genetically identified set of neurons to monitor calcium activity using a two-photon laser scanning microscope.

Optogenetics: We express a channelrhodopsin variant and a calcium indicator in a genetically identified set of neurons. Only a small subset of neurons is stimulated while the activity of the entire population is recorded. To do this, we developed a technique allowing simultaneous imaging and stimulation.

Computational modeling: A fundamental understanding of computational principles underlying complex neural dynamics does not come just from phenomenology, but from quantitative formulation. We develop dynamical models of the fly's navigational system and test their predictions using physiological tools such as two-photon imaging and optogenetics.

Circuit reconstruction using electron microscopy data: Recent progress in AI-assisted tracing methods, such as Flywire allows fast reconstruction of neural circuits using electron microscopy data. We use this resource to proofread and reconstruct the entire network structure of our interest. This information constrains the computational model space describing neural network dynamics and helps generate structurally informed predictions that our lab tests physiologically.



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A. Research Focus and established resources/techniques:

Molecular and cellular studies of brain injury, depression and neurodegenerative diseases using transgenic mouse models, tissue cultures and human samples.

Various cell type-specific WAVE1 or Ahnak KO lines.

Cell-type-specific TRAP (Translating Ribosome Affinity Purification)/RNA-seq: Parvalbumin-expressing interneuron-specific TRAP/RNA-seq, Endothelial cell-specific TRAP/RNA-seq.

- ***The function of Ahnak/p11/Anxa2 protein complex in neurons and vascular endothelial cells and its relevance to brain injury, depression or neurodegenerative diseases*** The goal of this project is elucidating roles of Ahnak pathways in the development of brain disorders and comorbidities, and thereby identifying novel disease mechanisms and therapeutic targets (Tools and/or mouse models - PMID: 23415230, 26370144, 30760886, 35813065)
- ***WAVE1 function in neurons and non-neuronal cells and its relevance to brain injury or neurodegenerative diseases.*** The goal of this project is elucidating protective roles of WAVE1 inhibition in brain injury or in the development of Alzheimer's disease. The mid or long term goal is to develop therapeutic approaches (Tools and/or mouse models - PMID 16862120, 20403076, 26280122, 28115704)
- ***Parvalbumin-expressing interneurons in stress-induced or hypoxic brain injury and its relevance to depression, epilepsy and neuropsychiatric disorders.*** The immediate goal of our research is identifying alterations of parvalbumin-expressing interneurons in chronic stress or hypoxia-induced brain injury and their relevance to neurological or neuropsychiatric disorders. The mid or long term goal is identifying novel disease mechanisms and therapeutic targets (Tools and/or mouse models - PMID: 35813065)

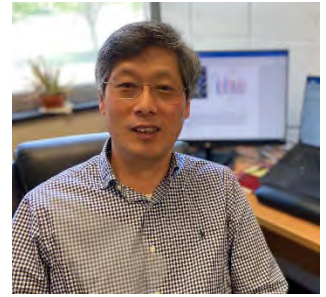
B. Techniques of interest: O-link or Somalomic proteomics, scRNA-seq-related applications, Spatial transcriptomics, Cell-type-specific metabolomics

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A. Research Interests

1. Targeting cellular senescence markers for therapeutic intervention in PD pathology:

Our recent publication in collaboration with the Ko lab at Johns Hopkins suggests that α -syn preformed fibrils (PFF)-induced pathology could lead to astrocyte and/or microglia senescence in PD brains, which may contribute to Parkinson's disease (PD) neuropathology (Verma et al., 2021). Targeting senescent cells using senolytics could therefore constitute a viable therapeutic option for the treatment of PD. As a follow-up study, we test the hypothesis that cellular senescence processes result in the failure of maintaining the homeostasis in dopamine neurons or surrounding astrocytes/microglia, which is associated with PD pathology. With measuring the levels of senescence markers in the PD-related regions including the striatum and Substantia nigra from PFF-injected PD mouse model or human PD brains, we can determine the effects of cellular senescence on inducing dopaminergic neuronal loss and PD pathology and verify the validity of using senolytics in halting the disease progression. This study will allow us to understand the senescence aspects of neuropathology of PD, which may reveal potentially new therapeutic targets using senolytics for preventing neurodegeneration including PD.

2. Oxidative stress increases the levels of deSUMOylation in PD related proteins for inducing PD pathology: We turned our efforts to determine if higher levels of SUMO proteases (SENPs) play a critical role in inducing pathological conditions in the striatum and midbrain from human PD tissues, compared to age-matched normal brains. We found that the level of SENP1 in human PD patient brains was higher than that in age-matched controls (a manuscript in prep). Thus, we set up a hypothesis that the level of SENP1 and its activity are stimulated by oxidative stress, which is a part of pathological mechanisms of PD. Our preliminary results demonstrated that MPTP- or PFF-induced oxidative stress removes SUMO1 from α -synuclein in mouse striatum and midbrain, while SUMO conjugase, Ubc9 overexpression-mediated SUMOylation protects the dopaminergic neurons in the striatum and Substantia Nigra against the toxicities (Verma et al., eNeuro, 2020). In addition, we found that SENP1 inhibition protects dopaminergic neurons in the striatum and SNc in PFF-injected mice. We also expect to see that higher levels of SENP1 in the Lewy bodies than those in normal brainstem tissues. Since high levels of SENP1 is associated with PD pathology in the human and mouse brains, the SENP1 inhibition can be a novel therapeutic target in PD pathology.

B. Common Lab techniques: Western blot, qRT-PCR, cell viability/cytotoxicity assays (MTT & LDH), ELISA, protein activity assays (including DAT, HAT & HDAC), ROS measurements, Protein aggregation (Thioflavin T) assay, primary neuron/astrocytes/microglia culture, microarray, Immunoprecipitation, immunohistochemistry, confocal microscopy, stereology, and Mass Spectrometry & MS imaging (collaboration).

C. Techniques of Interest

Mass-Spectrometry brain imaging (Bruker), single-cell Seq or MS, and midbrain-derived organoids culture.

D. NIH Study section

ADRD, CMND, CDIN and NOMD.



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A. Research Focus and Established Techniques: *Aging and oxidative stress-mediated alterations in gene regulation, mutagenesis, and pathogenesis of Neurodegenerative diseases manly focusing on Parkinson's disease and Alzheimer's disease.*

- **Transcriptional mutagenesis of oxidative DNA lesions in protein aggregation and neurodegeneration.** We have recently discovered that 8-oxo-dG, the most frequent oxidative DNA lesion, can generate mutant mRNA species by the intriguing mechanism called transcriptional mutagenesis, contributing to protein aggregation and pathogenesis of PD and AD. (PMID: 37740734)
- **Aging, Oligodendrocytes, and Microglia in PD: perspective from single-nucleus Multiomic analysis.** Aging is a major risk factor contributing to PD pathogenesis. The combined snRNA-seq and snATAC-seq analysis on young, aged, and PD postmortem midbrain reveals that oligodendrocytes and microglia change during aging and further contribute to PD pathogenesis. Peak-gene association analysis reveals the cell-type-specific contribution regarding which PD-associated SNPs may play roles in the pathogenesis. (PMID: 38491288)
- **The Gut-Brain Axis in Parkinson's disease.** The 'gut hypothesis for PD pathogenesis,' suggests that disturbances in the intestinal environment such as dysbiosis of gut microbiome trigger α -synuclein aggregation, which then propagates into the brain. Our laboratory is working on establishing novel mouse models of PD and dementia with Lewy body (DLB) that replicate dysbiosis and α -synuclein pathology in the gut, subsequently propagating into the brain

B. Techniques of interest: Electrophysiology combined with transcriptomic analysis, Neuroimaging

Poster #1

Macrophage-induced vascular smooth muscle cell apoptosis triggers intracerebral hemorrhage in mutant KRAS-induced brain arteriovenous malformations

Hyejin Park, Ph.D., Peng R. Chen, M.D., Eunhee Kim, Ph.D., Eun S. Park, Ph.D.

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Introduction: Brain arteriovenous malformation (bAVM)-caused intracerebral hemorrhage (ICH) is associated with disability or death. While the efforts to find the cause of bAVM-associated ICH continue, the role of macrophages, frequently found around bAVMs, is still unclear. Robust distribution of macrophages is detected in bAVMs, developed by overexpression of somatic mutation of KRAS mutation in endothelial cells (ECs). Given the evidence from the literature that infiltrated/activated macrophages cause the death of vascular smooth muscle cells (VSMC) through macrophage-expressing GPNMB and SPP1, the macrophage could initiate or accelerate the blood-brain barrier (BBB) impairment and subsequent ICH in bAVM.

Hypothesis: Our hypothesis is that activated/infiltrated macrophages drive apoptosis of VSMCs, resulting in BBB impairment and ICH occurrence in bAVMs.

Methods: We delivered AAV/BR1-KRAS (G12V) to brain ECs *via* retro-orbital venous sinus injection in mice to induce bAVM/ICH. Magnetic resonance imaging (MRI) was used to identify bAVM-caused ICH 8 weeks post-AAV injection. We determined the apoptosis of VSMC in bAVM and performed immunohistochemistry to validate the macrophage-expressing GPNMB and SPP1, which were identified by single-cell RNAseq.

Results: We found the increased expression of cleaved caspase-3 in α -smooth muscle actin-positive (+) VSMCs in bAVM territory. We also observed that iba1+ macrophages engulf the apoptotic VSMC in mice. We further confirmed that GPNMB and SPP1 were highly detected in ruptured bAVM compared to the unruptured bAVM. Interestingly, iba1+ macrophages highly express the GPNMB around ruptured bAVM compared to the unruptured bAVM. MRI and Ter-119 immunostaining confirmed the presence of bAVM rupture and ICH at sites where GPNMB and SPP1 are highly expressed.

Conclusion: Our data suggest macrophage-expressing GPNMB and SPP1 are associated with VSMC apoptosis around bAVM. Further studies will determine the detailed mechanism by which GPNMB and SPP1 cause VSMC apoptosis, BBB weakening, and ICH occurrence in mutant KRAS-induced bAVM.

Poster #2

Functional reorganization of brain-spinal connectivity after paralysis using transcutaneous spinal stimulation and upper limb motor training

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Background: Paralysis of the upper-limb (UL) caused by spinal cord injury (SCI) or stroke results in a significant loss of independence in an individual's daily life. Non-invasive, transcutaneous spinal stimulation (TSS) is a novel electrical neuromodulation strategy that has the potential to increase the excitability of spinal circuits and facilitate functional recovery after SCI or stroke. **Hypothesis:** We hypothesized that critical and functional reorganization of the brain and spinal cord interface after paralysis can be enhanced by functional UL and hand movements, in combination with TSS. **Methods:** Eight participants with tetraplegia due to SCI and five participants after stroke were recruited in this study. The interventions included sham stimulation or actual TSS, with a 2-week washout/rest period between phases. TSS waveforms consisted of biphasic 0.5 ms pulses, at a frequency of 10-90 Hz, applied between C3 and T1 vertebrae. Stimulation intensity was adjusted to motor threshold level to enable maximal performance during maximum voluntary contractions. The motor function in the affected upper arm, forearm, and wrist muscles was trained and evaluated using a robotic UL exoskeleton, with hand grip strength was trained and measured via a hand grip dynamometer. To assess changes in the spinal and corticospinal excitability after intervention, recruitment curves of spinal (sMEP) and corticospinal motor evoked potentials (cMEP) were obtained.

Results/Discussion: We found that TSS combined with UL motor training improved maximum voluntary contraction in affected muscles in the participants who had residual muscle responses measured via electromyography. Improvement in hand grip force was observed in some participants (3 out of 7 with SCI; 2 out of 5 with stroke) following the intervention. The TSS intervention reduced sMEP motor threshold and increased cMEP amplitude in tested hand muscles for the majority of stroke participants, whereas individuals with SCI did not show improvement in cMEP amplitude. Furthermore, one stroke participant exhibited improvement in muscle tone in the forearm flexor muscle post-intervention. **Conclusion:** We demonstrated that TSS in conjunction with motor training can improve volitional motor output in UL and hand muscles. This combined intervention holds the potential to augment corticospinal and spinal network function, particularly when administered alongside intense volitional training. Despite the small sample size, our preliminary findings suggest that this combined approach may be effective in restoring some degree of UL and hand motor function following paralysis.

Poster #3

Right Place and at the Right Time: Generation of disease-causing mutation G51D alpha-synuclein KI mice to learn the precise ontogeny of Parkinson's disease pathogenesis.

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Parkinson's disease (PD) is typically a sporadic late-onset disorder, which has made it difficult to model in mice. Several transgenic mouse models bearing mutations in *SNCA*, which encodes alpha-synuclein (α -Syn), have been made, but these lines do not express *SNCA* in a physiologically accurate spatiotemporal pattern, which limits the ability of the mice to recapitulate the features of human PD. Here we generated knock-in mice bearing the G51D *SNCA* mutation. After establishing that their motor symptoms begin at 9 months of age, we then sought earlier pathologies. We assessed the phosphorylation at Serine 129 of α -Syn in different tissues and detected phosphor- α -Syn in the olfactory bulb and enteric nervous system at 3 months of age. Olfactory deficit and impaired gut transit followed at 6 months, preceding motor symptoms. The *Snca*^{G51D} mice thus parallel the progression of human PD and will enable us to study PD pathogenesis and test future therapies.

Poster #4

Trametinib improves intracerebral hemorrhages in *KRAS*^{G12V}-induced brain arteriovenous malformations in mice

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Abstract: Brain arteriovenous malformations (bAVMs) are a major risk factor of cerebral hemorrhages in young patients. Recent clinical studies have reported that human bAVMs harbor somatic *KRAS* mutations (~76%), and the causal role of endothelial *KRAS* mutations in bAVM development were confirmed using animal models. Among *KRAS* downstream signaling, ERK was mainly activated in the mutant *KRAS*-induced bAVMs, and the MEK inhibition prevent the mutant *KRAS*-induced bAVMs. The results suggest that the RAF/MEK/ERK is the major pathway mediating the mutant *KRAS*-induced bAVMs. However, it is not clear the treatment efficacy of targeting RAF/MEK/ERK signaling in bAVMs. In the current study, we treated a FDA-approved MEK inhibitor, trametinib, into mice with bAVMs induced by brain endothelial-specific *KRAS*^{G12V} overexpression (*KRAS*^{G12V/bEC} mice) and determined body weight, mortality, hemorrhages, and the bAVM number and size changes. Trametinib did not alter the body weight during the treatment. We observed that the *KRAS*^{G12V/bEC} mice treated with vehicle eventually died; however, trametinib significantly improved the mortality rate suggesting that the trametinib treatment effectively reduced severe hemorrhages by bAVM rupture. Our longitudinal observation of the mouse bAVMs using non-invasive magnetic resonance imaging and angiogram showed that small hemorrhages were altered during the treatment period. However, there was no significant change of bAVM number or size in the mice. Our data show that inhibition of RAF/MEK/ERK by trametinib at least prevents the bAVM rupture. It suggests that targeting *KRAS* signaling may be a promising approach to treat bAVM patients.

Key words: brain arteriovenous malformations, *KRAS* mutation, RAF/MEK/ERK signaling, Trametinib.

Poster #5

Learning-associated astrocyte ensembles regulate memory recall

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**Contributed equally*

The physical manifestations of memory formation and recall are fundamental questions that remain unresolved. At the cellular level, ensembles of neurons called engrams are activated by learning events and control memory recall. Astrocytes are in close proximity to neurons and engage in a range of activities that support neurotransmission and circuit plasticity. Moreover, astrocytes exhibit experience dependent plasticity; however whether specific ensembles of astrocytes participate in memory recall remains obscure. Here we show that learning events induce c-Fos expression in a subset of hippocampal astrocytes, which subsequently regulates hippocampal circuit function. Intersectional, c-Fos based labeling of these astrocyte ensembles after learning events reveals that they are closely affiliated with engram neurons, while re-activation of these astrocyte ensembles stimulates memory recall. At the molecular level, these astrocyte ensembles exhibit elevated expression of NFIA and its selective deletion from this population suppresses memory recall. Together, our studies identify learning-associated astrocyte ensembles as a new form of plasticity that is sufficient to provoke memory recall, while implicating astrocytes as a reservoir for the storage of memories.

Poster #6

The neuron-immune-glioma crosstalk in glioblastoma multiforme (GBM) via immunoproteasome

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Glioblastoma multiforme (GBM), the deadliest cancer, hinders the success of innovative immunotherapies like ICIs and CAR-T cells due to its highly immunosuppressive microenvironment. To enhance anti-tumor immune responses against GBM, it's essential to thoroughly understand the mechanisms that shape the GBM immune microenvironment. Unlike other types of cancer, GBM is surrounded by a large number of active neurons. Our recent study showed that neuronal activation drives GBM growth and infiltration via neurotransmitter signaling and axon guidance pathways. Given that the characteristics of immune microenvironment is determined by the network between immune cells and various components of tumor microenvironment (TME), neuron may influence the distinctive immune TME of GBM. However, the dynamic interplay between neurons and the immune TME, and its impact on GBM progression, remain unexplored to date. In our previous study showing that contralateral neuronal hyperactivation leads to GBM infiltration, we observed that neuronal activity influenced GBM's immune microenvironment by activating microglia and rapidly recruiting macrophages and exhausted T cells. Given this preliminary data, we hypothesize that neurons regulate the GBM immune microenvironment, representing another significant mechanism in the vicious cycle between neurons and glioma cells. Here, we confirmed that contralateral neuronal activation significantly increased the number of activated tumor-associated microglia/macrophages (TAMs). We also showed that neuronal activation had limited impact on glioma infiltration and proliferation when TAMs were depleted, suggesting TAMs contribute to neuronal activation-dependent glioma infiltration. Furthermore, gliomas exhibit unique gene expression profiles in response to neuronal activation, potentially altering immune responses, including the activation of TAMs and infiltrated T cells. Notably, the Type 1 IFN signaling pathway, particularly immunoproteasome subunits (Psm8, Psm9, Psm10), was significantly upregulated in tumors following contralateral neuronal activation. Treatment with the immunoproteasome inhibitor, ONX-0914, significantly reduced tumor growth and infiltration, indicating its protumorigenic effect. Furthermore, immunoproteasomes in the tumor may influence the immune tumor microenvironment (TME), potentially contributing to the regulation of GBM immune responses via the neuron-tumor network. Collectively, our studies suggest that glioma infiltration driven by neuronal activation depends on activated TAMs. Moreover, we propose that the Type 1 IFN signaling pathway, especially tumor-expressed-immunoproteasome, might play a role as a molecular link in the neuron-immune-glioma network, thereby promoting glioma malignancy.

Poster #7

Home-cage assisted measurements of decision-making reveal deficits in *Mecp2*^{+/-} mice **Yoonhee Ki¹, Huda Zoghbi^{1, 2}, Nuo Li¹**

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Rett syndrome (RTT) is a neurodevelopmental disorder characterized by a wide range of symptoms, with severe apraxia being a notable feature. Apraxia is the inability to perform motor planning and is often associated with basal ganglia dysfunction. However, our knowledge of the circuit alterations in the basal ganglia and how they relate to the behavioral symptoms in RTT is limited. Here we used a novel approach to analyze circuit malfunction underlying behavior in a mouse model of RTT that carries a *methyl-CpG-binding protein 2* (*Mecp2*)-null allele (RTT mice).

In an automated home-cage system (Hao et al, eLife, 2021), self-motivated mice engaged in tactile decision-making tasks for over several months without human supervision. In the decision-making task, mice discriminated object location using whiskers and reported object location using directional licking. Parallel testing allowed us to assay two dozen cages at the same time. Instead of cross-sectional analysis, this approach longitudinally tracked the onset and progression of behavior deficits in the RTT mice over time relative to littermate wild-type (WT) mice. We discovered that RTT mice were able to learn the decision-making task similarly to WT mice at 12 to 16 weeks of age. However, RTT mice exhibited abnormal licking patterns and slower reaction time, which deteriorated with age. Once the mice achieved proficiency in the decision-making task, we conducted an additional assessment of their flexible motor planning by reversing the sensorimotor contingency. The new sensorimotor contingency allowed us to examine the mice's ability to adapt to new task rules. RTT mice exhibited slower reversal learning compared to WT mice at 16 to 20 weeks old. Over repeated sensorimotor reversals, both RTT and WT mice exhibited accelerated reversal learning. We are currently combining this approach with multi-Neuropixels probe recordings from a frontal cortico-basal-ganglia loop required for tactile decision-making. This loop includes anterior lateral motor cortex, lateral striatum, and ventromedial thalamus. Preliminary analyses suggest that there is reduced choice-related neural activity during decision-making in RTT mice.

Our study outlines a platform to assay motor planning deficits in the Rett mouse model and allows largescale analysis of the underlying neural dynamics.

Poster #8

Unveiling the Role of miR-183-5p in TDP-43 Proteinopathy: Implications for ALS Pathogenesis

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Background: Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disease characterized by the progressive degeneration of motor neurons, resulting in muscle weakness and eventual death. A prominent pathological feature of ALS is the misfolding, aggregation, and cytoplasmic mislocalization of TAR DNA-binding protein 43 (TDP-43) in a majority of patients, implicating TDP-43 proteinopathy in ALS pathogenesis. Mutations in SQSTM1/p62 have also been associated with both familial and sporadic ALS cases. Additionally, emerging evidence suggests that dysregulation of microRNAs (miRNAs) is linked to neuronal toxicity, mitochondrial dysfunction, and contributes to ALS pathogenesis.

Objectives: The study aimed to investigate the role of miR-183-5p in ALS pathogenesis and its potential regulatory mechanism involving SQSTM1/p62 and TDP-43.

Methods: The study utilized spinal cord samples from ALS patients to assess miR-183-5p expression levels. Luciferase reporter assays were conducted to confirm the interaction between miR-183-5p and the 3'-untranslated region of SQSTM1/p62. Additionally, the effects of miR-183-5p modulation were examined using miR-183-5p agomirs and antagomirs in neuronal and non-neuronal cell lines. Cellular responses, including changes in SQSTM1/p62 and TDP-43 protein levels, formation of stress granules, aggregation of TDP-43 protein, cytotoxicity, and total ubiquitination, were evaluated under various experimental conditions.

Results: The study revealed aberrant upregulation of miR-183-5p in the spinal cords of ALS patients. Luciferase reporter assays confirmed that miR-183-5p targets the 3'-untranslated region of SQSTM1/p62, resulting in its suppression. Treatment with miR-183-5p agomirs decreased SQSTM1/p62 expression and increased TDP-43 protein levels, while miR-183-5p antagomirs had the opposite effect. The antagomir treatment inhibited stress granule formation and aggregated TDP-43 protein under stress conditions, providing protection against cytotoxicity. Knockdown of SQSTM1/p62 decreased total ubiquitination and increased TDP-43 protein aggregation, suggesting a potential protective role of SQSTM1/p62.

Conclusion: This study elucidates a novel mechanism of TDP-43 proteinopathy mediated by miR-183-5p dysregulation. The findings provide insight into the molecular link between aberrant RNA processing and protein degradation, which are crucial processes in ALS pathogenesis.

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Poster #9

Regulation of headache response and transcriptomic network by the trigeminal ganglion clock

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Objective: To characterize the circadian features of the trigeminal ganglion in a mouse model of headache. Background: Several headache disorders, such as migraine and cluster headache, are known to exhibit distinct circadian rhythms of attacks. The circadian basis for these rhythmic pain responses, however, remains poorly understood.

Methods: We examined trigeminal ganglion ex vivo and single-cell cultures from Per2::LucSV reporter mice and performed immunohistochemistry. Circadian behavior and transcriptomics were investigated using a novel combination of trigeminovascular and circadian models: a nitroglycerin mouse headache model with mechanical thresholds measured every 6 h, and trigeminal ganglion RNA sequencing measured every 4 h for 24 h. Finally, we performed pharmacogenomic analysis of gene targets for migraine, cluster headache, and trigeminal neuralgia treatments as well as trigeminal ganglion neuropeptides; this information was cross-referenced with our cycling genes from RNA sequencing data to identify potential targets for chronotherapy.

Results: The trigeminal ganglion demonstrates strong circadian rhythms in both ex vivo and single-cell cultures, with core circadian proteins found in both neuronal and non-neuronal cells. Using our novel behavioral model, we showed that nitroglycerintreated mice display circadian rhythms of pain sensitivity which were abolished in arrhythmic Per1/2 double knockout mice. Furthermore, RNA-sequencing analysis of the trigeminal ganglion revealed 466 genes that displayed circadian oscillations in the control group, including core clock genes and clock-regulated pain neurotransmitters. In the nitroglycerin group, we observed a profound circadian reprogramming of gene expression, as 331 of circadian genes in the control group lost rhythm and another 584 genes gained rhythm. Finally, pharmacogenetics analysis identified 10 genes in our trigeminal ganglion circadian transcriptome that encode target proteins of current medications used to treat migraine, cluster headache, or trigeminal neuralgia

Poster #10

CIC isoforms have differential functions that are critical for survival and brain development

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Capicua (CIC) is a transcription factor which forms a co-repressor complex with either Ataxin1 (ATXN1) or its paralog, Ataxin1-like (ATXN1L), to repress target gene expression. Our lab has demonstrated that the gain of function of the ATXN1-CIC complex drives Purkinje cell degeneration in spinocerebellar ataxia type1. Conversely, complete loss of function of this complex leads to perinatal lethality demonstrating that it is essential for survival. Additionally, heterozygous loss of *CIC* function in humans leads to a neurodevelopmental disorder known as *CIC* haploinsufficiency syndrome (CHS) characterized by intellectual disability, autism, seizures, and ADHD. CIC is evolutionarily conserved from fruit flies to humans and has two major isoforms, CIC-L (long) and CIC-S (short), which are generated by alternative promoter use. While the known DNA binding domains are shared between the two isoforms, CIC-L has an additional 931 unique amino acids while CIC-S has 22 unique amino acids. Recently, we have identified eight patients with de-novo variants in CIC-L who display symptoms of CHS. Thus, given the importance of CIC in survival, neurodevelopment, and the identification of CIC-L-specific coding variants, we set out to understand the importance of each CIC isoform.

To investigate the functional consequences of loss of each isoform of CIC, we generated CIC-L and CIC-S isoform-specific knock-out (KO) mice using CRISPR/Cas9. Interestingly, CIC-S-KO mice have reduced survival at weaning, but CIC-L-KO does not lead to premature lethality. Conversely, behavioral analysis in surviving adult mice demonstrates that CIC-L- KO mice have impaired learning, memory, and motor coordination, but CIC-S-KO do not exhibit these behavioral phenotypes. To understand the molecular mechanism of the isoform-specific phenotypes, we first examined the expression pattern of both isoforms during postnatal development and determined that CIC-S is higher in early development while CIC-L increases as animals mature. Further, we performed IP-MS to identify unique interactors for each isoform and validated a unique interactor of CIC-S. We plan to perform transcriptomic analysis to determine whether there are unique gene signatures that are driving isoform-specific phenotypes. Studying the role of the two CIC isoforms will not only help advance our understanding of the biology of CIC but will also provide insights into the contributions of each isoform to various human disorders.

Poster #11

Beyond the Brain: Alzheimer's Disease's Unforeseen Impact on the Peripheral System

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Alzheimer's disease (AD) is a devastating, progressive disorder, the burden of which has global negative impacts. Currently, there is no effective treatment for AD, and recent advances only have mild impacts on slowing cognitive defects. AD has been heavily studied for pathological changes and cellular mechanisms that disrupt the nervous system, primarily neurons. Intriguingly, there is growing interest in understanding the interplay between AD and the periphery in the context of aging. As such, AD has been connected to disruptions in the gut microbiome, respiratory system, cardiovascular function, and hormone homeostasis, supporting that peripheral tissues are also involved in disease. However, a causal relationship between AD progression and peripheral dysregulation is not well established. Here, we aim to systematically investigate how AD progression impacts an entire organism at cellular resolution using *Drosophila* and a single-cell atlas approach.

Poster #12

Role of Endogenous Dopamine Signaling in the Lateral Parabrachial Nucleus in Somatosensation

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The lateral parabrachial nucleus (LPBN), a crucial hub for integrating and modulating diverse sensory information, is known to express both D1 and D2 dopamine receptors and receive dopaminergic inputs. However, the role of this LPBN dopaminergic system in somatosensory processing remains largely unexplored. This study investigated if mechanical sensory stimulation triggers dopaminergic signaling in the LPBN and how blocking the D1 and D2 receptors in the LPBN affects mechanosensitivity at a behavioral level in mice. We measured the levels of dopaminergic signaling with a G-protein-coupled receptor-based dopamine sensor in the LPBN and assessed withdrawal responses to mechanical stimulation after unilaterally microinjecting either D1 or D2 receptor antagonist into the PBN. In awake, freely moving mice, a noxious pinch, but not a gentle stroking, increased dopaminergic signaling in the LPBN. The D1 receptor antagonist SCH 23390, at a 0.1 μg dose, significantly heightened mechanosensitivity in females and showed a trend toward increased mechanosensitivity in males. Conversely, the D2 receptor antagonist Eticlopride, at doses of 0.3 and 1 μg , suppressed mechanosensitivity in both sexes. Notably, a 1 μg dose of Eticlopride in the LPBN markedly attenuated mechanical hypernociception in a capsaicin-injected hind paw. These results suggest that endogenous dopaminergic signaling occurs in the LPBN upon noxious mechanical stimulation, inhibiting mechanosensitivity through D1 receptors while enhancing it through D2 receptors. The D2 receptor in the LPBN may play a role in an injury-induced increase in mechanical nociception. Therefore, inhibiting D2 receptor signaling in the LPBN could offer potential as an analgesic strategy.

Poster #13

A *de novo* gain-of-function variant in the *BMPR2* gene induces neurodevelopmental abnormalities

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The loss-of-function (LoF) in the Bone Morphogenetic Protein Receptor Type 2 (*BMPR2*) has been identified as a significant factor contributing to pulmonary arterial hypertension (PAH). However, until now, no other human diseases have been linked to *BMPR2*, despite the BMP pathway's crucial role in tissue development across various organisms. Recently, we discovered four patients with an identical heterozygous *BMPR2* variant (p.E376K), all exhibiting neurodevelopmental phenotypes, including autism spectrum disorder (ASD) and intellectual disability (ID), without presenting PAH. This suggests that the p.E376K variant might possess unique properties differing from the LoF alleles previously associated with *BMPR2*.

Utilizing the *Drosophila* model, we developed transgenic fly lines expressing various human *BMPR2* proteins, including the *BMPR2* reference, *BMPR2* p.E376K, and PAH-associated variants (*BMPR2* p.C420Y and *BMPR2* p.R491W). Overexpression of *BMPR2* p.E376K notably hyperactivated the fly's BMP signaling pathway, resulting in significant developmental defects across multiple tissues. In contrast, overexpression of the *BMPR2* reference protein induced only mild phenotypes, and the PAH variants caused no noticeable phenotypes. This pronounced difference strongly indicates that the *BMPR2* p.E376K variant displays gain-of-function (GOF) characteristics. Further analysis showed that this variant activates BMP signaling in a ligand-independent manner yet requires the type 1 receptor.

In neuronal tissues, the impact of the p.E376K variant exhibited remarkable specificity. Expression in neurons led to BMP signaling activation confined to certain neuron types, such as Da neurons, correlating with the relatively mild patient phenotypes observed. Conversely, expression in glial cells caused extensive BMP signaling activation, resulting in lethality. Furthermore, expressing the *BMPR2* p.E376K variant in neuroblast cells led to severe lethality, with survivors living significantly shorter lives compared to those expressing the *BMPR2* reference. The differential responses across neurons, glia, and neuroblast cells highlight the variant's unique, cell-type-specific effects, suggesting a significant contribution of the *BMPR2* p.E376K gain-of-function allele to the clinical phenotypes observed in patients.

Poster #14

MeCP2 interacts with the super elongation complex to regulate gene expression

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Methyl CpG binding protein 2 (MeCP2) is an epigenetic reader in the brain that globally binds to methylated cytosines on the DNA and fine-tunes gene expression. One of the proposed mechanisms by which MeCP2 regulates gene expression is by repression of transcription via recruitment of repressors such as the NCoR and Sin3A complexes.

However, gene expression studies revealed that *Mecp2* null mice have many down-regulated genes, the same genes that are up-regulated in a MeCP2 overexpression mouse model, suggesting that MeCP2 can also activate gene expression. To better understand the mechanisms by which MeCP2 regulates gene expression, we set out to find chromatin factors that genetically interact with *MECP2*. Performing a genetic modifier screen in *Drosophila*, we found previously identified protein interactors including components of the NCoR, Sin3A, and SWI/SNF complexes as genetic modifiers of MeCP2 toxicity. Interestingly, we also found that components of the super elongation complex (SEC), a transcriptional activator complex, genetically interact with *MECP2*. We further validated the physical interaction between MeCP2 and the SEC and found that the loss of MeCP2 leads to the decrease in binding of AFF4, the scaffold of the SEC, on a subset of genes in the mouse cortex. Further, we show an enrichment of genes in the same subset that have decreased binding of RNA polymerase II and gene expression. Taken together, our study uncovers a novel molecular axis MeCP2 utilizes to regulate gene expression.

Poster #15

Stool Shotgun Metagenomic Analysis Reveals Gut Microbial Characteristics Associated with Dementia with Lewy Bodies

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Background: Dementia with Lewy bodies (DLB) is the second most common neurodegenerative dementia worldwide. Idiopathic rapid-eye-movement sleep behavior disorder (iRBD) is one of the earliest and most specific prodromal indicators of DLB, with one in four iRBD patients converting to DLB. Recent studies have suggested that the gut-brain axis potentially links the gut microbiome with the progression of several neurological disorders. In this study, we aim to improve our understanding of the role of the gut microbiome in the development of DLB by identifying bacterial species and strains associated with DLB and iRBD.

Method: Stool samples were collected from 25 patients with DLB, 10 with iRBD, and their household- paired controls. Whole genome shotgun (WGS) metagenomes of all samples were analyzed using the MetaPhlAn 4.0 and the HUMAnN 3.0 pipelines for taxonomic and functional profiling, respectively. Furthermore, strain-level analysis of bacterial species that were differentially prevalent between study groups was performed using StrainPhlAn 4.0.

Results: Gut microbiomes of DLB patients had a significantly lower Simpson's diversity index than controls ($P < 0.05$), while there was no difference in this diversity index between iRBD patients and controls. Compared to the controls, DLB and iRBD patients showed significantly increased relative abundance in 4 and 9 bacterial species, respectively ($P < 0.05$), such as *Odoribacter laneus*, *Oscillibacter* sp. CAG:241, *Collinsella aerofaciens*, and *Anaeromassilibacillus* sp. An250. 6 and 21 biochemical pathways were associated with DLB and iRBD, such as L-methionine Biosynthesis and Pentose Phosphate Pathway, respectively ($P < 0.05$). The Gut Microbiome Wellness Index 2 (GMWI2), which evaluates the likelihood of disease presence independent of the clinical diagnosis based on a species- level taxonomic profile of a stool sample, was significantly lower in DLB patients compared to iRBD patients ($P < 0.05$).

Conclusions: This study represents the first shotgun metagenome analysis of stool samples from DLB and iRBD patients. We identified unique taxonomic and functional characteristics of the gut microbiome associated with DLB and iRBD, providing insights into the role of the gut-brain axis in this spectrum of neurodegenerative disorders.

Poster #16

Acid-degradable Lipid Nanoparticle-mediated Gene Editing Rescues Spatial Memory Deficits in the Mouse Model of Fragile X Syndrome

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Fragile X syndrome (FXS) is a common form of intellectual disability and the most common monogenic cause of autism. FXS is caused by transcriptional silencing of the fragile X messenger ribonucleoprotein 1 (*FMR1*) gene, and results in the absence of fragile X messenger ribonucleoprotein (FMRP). The silencing of FMRP in *Fmr1* KO mice recapitulates abnormal behaviors such as hyperactivity, repetition, and learning memory deficits seen in FXS patients. To rescue some of these behavioral phenotypes, we targeted the *Grm5* gene encoding mGluR5, which is associated with FXS. Here, we intracerebrally injected Cas9 mRNA/*Grm5* sgRNA using acid-degradable polyethylene glycol lipid nanoparticles (termed ADP-LNPs) to reduce the expression of mGluR5 in the hippocampus of *Fmr1* KO mice. First, we observed a local reduction of mGluR5 expression at injected sites in the hippocampus. Next, we demonstrated that spatial memory deficits associated with the hippocampus were rescued by Cas9 mRNA/*Grm5* sgRNA treatment. Finally, we demonstrated that injection of Cas9 mRNA/*Grm5* sgRNA into the hippocampus of *Fmr1* KO mice did not rescue abnormal hyperactivity and repetition since these behaviors correlate with brain regions other than the hippocampus. Overall, ADP-LNPs mRNA-mediated gene editing efficiently and locally affects the injected brain region and shows great promise as potential precision-medicine therapeutics.

Poster #17

Deciphering mechanisms of perinatal white matter injury-induced neuropsychiatric outcomes

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Perinatal white matter injury (pWMI) is the most common form of infantile brain injury associated with prematurity, maternal immune activation (MIA), and neonatal hypoxic-ischemic encephalopathy (HIE). Although neonatal death and chronic neurological morbidities such as cerebral palsy and intellectual disability are well-studied as sequelae of pWMI, there is mounting evidence that pWMI may result in neuropsychiatric disorders, including attention deficit hyperactivity disorder, autism spectrum disorder, anxiety, depression, and schizophrenia. However, the mechanisms by which pWMI contributes to neuropsychiatric disorders remain poorly understood. To underpin pathophysiological mechanisms leading to neuropsychiatric outcomes in pWMI patients, we generated a mouse model induced by a combination of 1) MIA leading to fetal inflammation and 2) early postnatal hypoxia to simulate pathological conditions in humans. By performing a battery of behavioral assays, we found that mice under pWMI exhibit deficits in cognitive function, impaired social interaction, and depression indicating neuropsychiatric behaviors present in our pWMI mouse model. Importantly, these behavioral alterations were more noticeable in male mice than in female counterparts, suggesting sex-specific mechanisms may exist. In vivo DTI neuroimaging revealed abnormality of white matter integrity in multiple brain regions of pWMI-treated mice, correlating recent clinical studies that deformity in white matter is apparent in a wide range of neuropsychiatric disorders patients. In order to address changes triggered by pWMI at the cellular level, we conducted single nuclei RNA sequencing and found significant modification in oligodendrocytes and excitatory neuronal populations by cell composition analysis and differentially expressed gene analysis. The decrease in mature oligodendrocytes and delayed myelination were further confirmed by histological analysis. Because myelination is imperative for brain circuit refinement and subsequent behavior, we examined changes in neuronal activity and found a brain region-specifically diminished c-fos activity. Electrophysiological evaluation of neuronal activity also revealed impaired synaptic transmission by pWMI. Collectively, we successfully established the model of pWMI-induced neuropsychiatric disease, and our results highlight the significance of white matter health and function for neuropsychiatric disease pathogenesis. Unraveling the interaction between oligodendrocytes and neurons and pinpointing crucial players through deeper analysis of DEGs will elucidate the mechanisms through which pWMI contributes to neuropsychiatric disorders.

Poster #18

Therapeutic functions of astrocytes to treat α -synuclein pathology in Parkinson's disease

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Intraneuronal inclusions of misfolded α -synuclein (α -syn) and prion-like spread of the pathologic α -syn contribute to progressive neuronal death in Parkinson's disease (PD). Despite the pathologic significance, no efficient therapeutic intervention targeting α -synucleinopathy has been developed. In this study, we provide evidence that astrocytes, especially those cultured from the ventral midbrain (VM), show therapeutic potential to alleviate α -syn pathology in multiple in vitro and in vivo α -synucleinopathic models. Regulation of neuronal α -syn proteostasis underlies the therapeutic function of astrocytes. Specifically, VM-derived astrocytes inhibited neuronal α -syn aggregation and transmission in a paracrine manner by correcting not only intraneuronal oxidative and mitochondrial stresses but also extracellular inflammatory environments, in which α -syn proteins are prone to pathologic misfolding. The astrocyte-derived paracrine factors also promoted disassembly of extracellular α -syn aggregates. In addition to the aggregated form of α -syn, VM astrocytes reduced total α -syn protein loads both by actively scavenging extracellular α -syn fibrils and by a paracrine stimulation of neuronal autophagic clearance of α -syn. Transplantation of VM astrocytes into the midbrain of PD model mice alleviated α -syn pathology and protected the midbrain dopamine neurons from neurodegeneration. We further showed that cografting of VM astrocytes could be exploited in stem cell-based therapy for PD, in which host-to-graft transmission of α -syn pathology remains a critical concern for long-term cell therapeutic effects.

Poster #19

Abnormal Ciliogenesis in FMRP-deficient Models is Rescued by HDAC6 Inhibition

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Fragile X syndrome (FXS) is a common form of intellectual disability and the most common monogenic cause of autism. FXS occurs as a result of fragile X messenger ribonucleoprotein 1 (*FMR1*) gene hypermethylation due to the CGG repeat expansion (> 200 repeats), which leads to transcriptional silencing and the absence of fragile X messenger ribonucleoprotein (FMRP), a translational regulator. Primary cilia are specialized, microtubule-based structures projecting from the surface of most mammalian cells. These organelles are thought to primarily act as signaling hubs and sensors. Defective primary cilia function or structure is responsible for a group of disorders collectively termed ciliopathies. Given the known shared phenotypes between losing primary cilia and losing FMRP in the brain, investigating whether primary cilia contribute to FXS pathophysiology is important in understanding FXS. Notably, Lee lab previously reported primary ciliary deficits (number or length) in multiple brain regions including the dentate gyrus of the hippocampus and the cerebellum using FXS mouse model. Here, we investigate ciliogenesis and elucidate possible molecular mechanisms underlying primary ciliary deficits in the absence models of FMRP. We investigate the possible role of ciliogenesis in the brain based on our observations from FXS patient-derived cells. Our result demonstrates that primary cilia is reduced in FXS patient-derived fibroblast (FXS cell) and FMRP-silenced HEK293 cell. Next, we demonstrate that Tubastatin A (HDAC6 inhibitor) treatment rescues abnormal ciliogenesis in FXS cells. Lastly, we confirm the rescue of abnormal ciliogenesis by treating Tubastatin A in the cerebellum and dentate gyrus of *Fmr1* KO mice. These results indicate that HDAC6 is associated with abnormal ciliogenesis in the absence of FMRP.